

Vesicular Contact Reaction May Progress into Erythema Multiforme

Dear Editor,

Erythema multiforme is considered an acute skin condition, characterized by a self-limiting and sometimes recurrent course. It is regarded as a type IV hypersensitivity reaction associated with certain infections, medications, and other various triggers. Allergic contact dermatitis is in turn a delayed type of induced allergy as a result of cutaneous contact with a specific allergen to which the patient develops specific sensitivity. This type of cutaneous reaction is associated with inflammation manifesting with erythema, edema, and vesicles.

A 27-year old female patient presented with a 3-day history of erythematous and vesicular lesions which developed 24 hours after cesarean section. Initially the lesions were localized in the area of surgery (mainly the abdomen and upper thighs) and on the next day progressed to the buttocks and lumbar area. The patient was referred to the Outpatient Clinic and was treated with antihistamines, but her dermatological state deteriorated rapidly. At the day of admission to the Department of Dermatology, numerous erythematous and vesicular lesions were present on the skin of the abdomen, thighs, and back (Figure 1, a), but the skin of the neck, chest, and extremities was also covered with erythematous and edematous patches. On the second day of hospitalization, we observed the evolution of lesions localized within the chest and extremities into an erythema multiforme-like targetoid eruption (Figure 1, b).

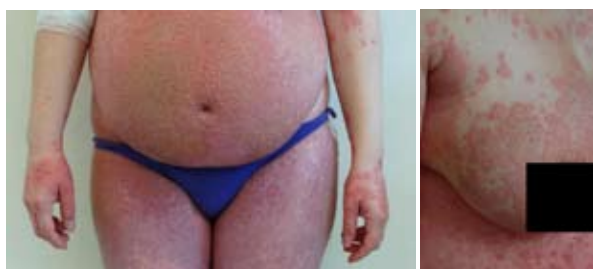


Figure 1. Erythematous and vesicular lesions on the abdomen and thighs (a) and targetoid lesions within the breast area (b).

Initially the patient was treated with intravenous injections of dexamethasone and ceftriaxone and orally with second-generation antihistamines (in four-fold doses), followed by intravenous metyloprednisolone pulse-therapy (total dose of 3 g). As the new vesicobullous lesions started to appear on the face and arms, we introduced cyclosporine A orally 400 mg daily. We could then observe gradual remission, but on the seventh day of hospitalization the patient developed a massive labial herpes simplex infection and had to be treated with acyclovir intravenously. Eight days after admission, we switched from intravenous metyloprednisolone to its oral formula.

Diagnostic methods included: laboratory analyses (leukocytosis, neutrophilia, lymphopenia could be observed, and also serum CRP elevation). Pemphigoid gestationis was excluded on the basis of a direct immunofluorescence from perilesional skin and on the basis of indirect immunofluorescence and also serum analysis using ELISA for serum IgG antibodies to



Figure 2. Patch test results – positive reactions to colophonium, fragrance mix, and formaldehyde (a) and a positive reaction to the disinfectant agent (b).

Table 1. Patch test results evaluated according to the International Contact Dermatitis Research Group (ICDRG)

Chemical	Concentration and vehicle	Result day 2	Result day 3
Colophonium	20% – white petrolatum	++	+++
Fragrance mix I	8% – white petrolatum	++	+++
Formaldehyde	1.00% – water	++	+++
Chloromethylisothiazolone	0.01% – water	++	+++
Balm of Peru	25% – white petrolatum	++	+++
Propolis	10% – white petrolatum	+++	+++
Kodan Tinctur forte	1:100 in water	+++	+++

BP180-NC16A (courtesy of Prof. Marian Dmochowski). Histopathological examination revealed: massive edema of dermal papillae, leading to the formation of sub-epidermal vesicles; individual cell necrosis was observed in the upper epidermis. Within the dermis, a dense, perivascular inflammatory infiltrate was detected: the clinical picture suggested erythema multiforme. Another histopathological examination was performed at the University Clinic of Dermatology and Venereology in Magdeburg, courtesy of Prof. Dr. Harald Gollnick and Dr. Med. I. Franke; it also suggested the bullous form of erythema multiforme (dermal type).

Three months after remission, the patient was hospitalized again to perform allergological diagnostics. Patch tests were performed with the European Baseline Series (Chemotechnique Diagnostics) supplemented with disinfectants and textiles used during surgical procedure. For patch testing, Finn Chambers on Scanpor were used. Results were recorded at 48 and 72 hour time points. According to the ICDRG (International Contact Dermatitis Research Group), reactions evaluated as ++ and +++ pluses were considered as positive and reaction evaluated as + plus was considered as doubtful. Patch testing revealed polyvalent contact allergy (Table 1), (Figure 2a). The patient also reacted to Kodan Tinctur forte used as a skin disinfectant (contains brown dye LF 1889 – mixture of quinoline yellow, sunset yellow, brilliant black) (Figure 2b). It has to be emphasized, that patch test reading procedure was difficult due to patient's skin reactivity toward a plaster mounting Finn chambers.

Literature data suggests that erythema multiforme may occasionally occur in conjunction with allergic contact dermatitis to various non-related substances including chemicals (epoxy-based compound, fragrances, epichlorhydrine, bromofluorene), medications (antibiotics, acetaminophen, triamcinolone, bufexamac), plant-derived allergens (poison ivy, tea tree oil, red cedar essential oil), but also rubber ingredients and nickel. The severity of the reaction var-

ies from mild erythema to generalized erythema multiforme or even toxic epidermal necrolysis (1,2,3,4). Lesions characteristic for erythema multiforme may appear during the episode of acute contact dermatitis or may follow a nearly resolving vesicular eczematous eruption. The pathomechanism of an erythema multiforme-like eruption developing in association with allergic contact dermatitis still remains unclear. Immune complex-mediated and T-cell-mediated reactions have been proposed as the cause. However, T-cell-mediated cellular mechanisms seems to be more likely, since generalized erythema multiforme often follows contact dermatitis, which is a type IV allergic reaction mediated by T cells (5,6).

According to Bushkell *et al.* (7), an allergen penetration through the skin may result in a type III hypersensitivity reaction, with involvement of circulating immune complexes, and to confirm that, IgM, IgA, C3, and fibrin deposits are detected in some cases of targetoid lesions in erythema multiforme. On the other hand, Wiedemeyer *et al.* (8) suggest that contact allergens (i.e. paraphenylenodiamine) may be transported in peripheral blood mononuclear cells from the area of initial skin contact even to distant sites. According to Shiohara *et al.* (9) and Gonzalez-Delgado *et al.* (10), epidermal expression of adhesion molecule – 1 (ICAM-1) and the number of CD4+ T cells is increased within the iris lesions of erythema multiforme. Thus, it is possible that adhesion molecules may facilitate epidermal invasion of lymphocytes in these lesions, which is also the place of the expression of maintained allergen molecules.

In conclusion, in the described case the causative factor also remained uncertain. The patient was found to have contact allergy to six haptens included in the European Baseline Series and also to a disinfectant used during cesarean section. Among these, both colophonium and formaldehyde are used in adhesives and glues or surface coatings. However, formaldehyde is mainly associated with this type of the reaction – in fact, hapten description supplied by

Chemotechnique Diagnostics includes the information that "formaldehyde may produce erythema multiforme-like eruptions".

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