Contact Dermatitis

Volume 57 Issue 5 Page 321-323, November 2007

To cite this article: Thomas Hohwy, Klaus Ejner Andersen, Henrik Sølvsten, Mette Sommerlund (2007)
Allergic contact dermatitis to methyl aminolevulinate after photodynamic therapy in 9 patients
Contact Dermatitis 57 (5), 321–323.
doi:10.1111/j.1600-0536.2007.01243.x

Prev Article Next Article

Full Text

Allergic contact dermatitis to methyl aminolevulinate after photodynamic therapy in 9 patients

- *Thomas Hohwy[11]Department of Dermatology and Allergy Center, Odense University Hospital, University of Southern Denmark, DK-5000 Odense, Denmark,*
- *Klaus Ejner Andersen[11]Department of Dermatology and Allergy Center, Odense University Hospital, University of Southern Denmark, DK-5000 Odense, Denmark,*
- *Henrik Sølvsten[22]Department of Dermatology, Aarhus University Hospital, P. P. Oerumsgade 11, DK-8000 Aarhus C, Denmark and*
- *Mette Sommerlund[22]Department of Dermatology, Aarhus University Hospital, P. P. Oerumsgade 11, DK-8000 Aarhus C, DenmarkMette Sommerlund*
  Aarhus University Hospital
  P. P. Oerumsgade 11
  8000 Aarhus C
  Denmark

  Tel: +4589491861
  Fax: +4589491860
  e-mail: rlg12mso@as.aaa.dk

- [1]Department of Dermatology and Allergy Center, Odense University Hospital, University of Southern Denmark, DK-5000 Odense, Denmark, and [2]Department of Dermatology, Aarhus University Hospital, P. P. Oerumsgade 11, DK-8000 Aarhus C, Denmark

Mette Sommerlund
Aarhus University Hospital

P. P. Oerumsgade 11
8000 Aarhus C
Denmark

Tel: +4589491861
Fax: +4589491860
e-mail: rlg12mso@as.aaa.dk

This report describes 9 patients who developed allergic contact dermatitis to methyl aminolevulinate used for photodynamic therapy (PDT). The risk of developing contact allergy to methyl aminolevulinate in PDT treated patients was calculated to 1% after an average of 7 treatments (range 2–21).

Photodynamic therapy using methyl aminolevulinate (Metvix®) as a photosensitizer was introduced in Denmark in 2002. It is now a routine procedure for use in treatment of actinic keratoses, Bowens disease and superficial basal cell carcinomas. Methyl aminolevulinate is applied to the lesional skin after a light curettage of superficial tumour and left under occlusion for 3 hr followed by exposure to red light. Methyl aminolevulinate is converted intracellularly to precursors of haem, with accumulation of protoporphyrin IX, which is an active photosensitizer activated by blue and red light. 2 cases of allergic contact dermatitis to methyl aminolevulinate has been published before (1, 2).

We report a series of 9 patients who developed severe acute allergic contact dermatitis during methyl aminolevulinate photodynamic therapy.

6 women and 3 men, age 31–70 years, suddenly developed an unexpected aggravated and spreading local inflammatory reaction at the treated skin site compatible with acute severe spreading dermatitis after varying number of treatments (Table 1). They complained of itching and pain from the treated area few hours after light exposure. Some patients developed symptoms within 1–2 days after photodynamic therapy (PDT) and were treated with antibiotics by their general physician, who suspected a local infection. 1 patient developed severe and was spreading oedema on the face (Fig. 1). Admission to the in-patient department and systemic treatment with prednisolone was indicated in 1 case. A contact allergic reaction to the methyl aminolevulinate cream was suspected.

After healing of the dermatitis, the patients were patch tested with Metvix® cream as is, and placebo cream kindly supplied by the manufacturer (PhotoCure AS, Oslo, Norway). Pure methyl aminolevulinate was not available. Standard patch test procedure with small Finn Chambers® (Epitest, Tuusula, Finland) on Scanpor® (Alpharma AS, Oslo, Norway) was used, and reading according to guideline.

The patient and patch test data are presented in Table 1. 8 of 9 patients had ++ to +++ reactions to MAL at the D3 reading, and 1 had a follicular reaction considered to of allergic nature. 25 consecutive controls were tested and showed 5 questionable reactions of macular erythema (+?) and no positive or obvious irritant reaction.

At the departments in Odense and Århus from January 2004 to October 2006 a total of 2755 PDT treatments were given to a total of 907 patients giving an average of 3 PDT treatments per patient and a calculated sensitization risk of 1% of treated patients and 0.3% of PDT treatments given.

The consistent strong positive patch test reactions to the Metvix cream, and negative reactions to the placebo cream is a strong indicator of sensitization to methyl aminolevulinate and not vehicle components. A compound allergy cannot be completely excluded as an explanation, but it is less likely. Unfortunately, pure methyl aminolevulinate was not available for patch testing. The cream contains ingredients, which in themselves may be rare contact allergens, such as cetostearyl alcohol and oleyl alcohol, and parabens as preservatives. The product information accompanying Metvixia registration in the USA, and published on the Internet, states that allergic reactions may occur as dermal safety studies in human volunteers have shown a considerable risk of sensitization. A provocative cumulative irritancy and sensitization study of Metvixia cream showed that 30 of 58 subjects, who agreed to challenge with Metixia cream were positive (sensitized).

This series of patients with allergic contact dermatitis to methyl aminolevulinate developed an unusual strong local reaction with pronounced spreading, itching, and oedematous dermatitis following PDT, which raised the suspicion of contact allergy. Some of our patients received additional PDT after they had had their first signs and symptoms of contact allergy, and they all developed severe and prolonged dermatitis reactions after the following treatments. We did not investigate the possible effect of red light on the methyl aminolevulinate test reaction. Photoaggravation was not suspected from the clinical picture.

Several patients received antibiotics by their general practitioner because of a suspicion of cellulitis.

The allergic reaction did not seem to have had any negative influence on the treatment results in our patients. However, most of the allergic patients experienced so severe dermatitis that PDT had to be discontinued. In our opinion, contact allergy to methyl aminolevulinate is an absolute contraindication to PDT treatment in the facial area because of the possible severe oedema accompanying the allergic reaction. Further PDT treatment on other parts of the body may be possible if alternative treatment modalities are less desirable; however, this has not been studied. The prevention of allergic reaction by pre-treatment with prednisolone is not investigated but it is a theoretical possibility. 5 patients with methyl aminolevulinate contact allergy were also patch tested with 5-aminolevulinate, which gave negative reactions so cross reactivity seems not to be present, in accordance with the information in the product information. The methylation of 5-aminolevulinic acid to methyl aminolevulinate and the administration in an optimized vehicle that seems to increase the risk of contact sensitization.

WulfH C, PhilipsenP. Allergic contact dermatitis to 5-aminolaevulinic acid methylester but not to 5-aminolaevulinic acid after photodynamic therapy. *Br J Dermatol* 2004: **150**: 143–145.

Synergy, Medline, ISI, Chemport

2.

HarriesM J, StreetG, GilmourE, RhodesL E, BeckM H. Allergic contact dermatitis to methyl aminolevulinate (Metvix®) cream used in photodynamic therapy. *Photodematol Photoimmunol Photomed* 2007: **23**: 35–36.