

LETTERS TO THE EDITOR

Pseudoleucoderma After Injections of Afamelanotide in a Patient with Atopic Dermatitis

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Alpha melanocyte stimulating hormone (alpha-MSH) is a 13-amino-acid pigmentary peptide hormone, which is synthesized in the pars intermedia of the pituitary gland by endoproteolytic decomposition of proopiomelanocortin. Upon exposure to ultraviolet (UV) radiation it is also produced by keratinocytes, melanocytes and macrophages (1). Alpha-MSH causes the dissemination of pigmented granules in the melanophores via G-Protein-linked receptors, leading to pigmentation of the skin and improvement of DNA repair in melanocytes. Due to its lipophilic property alpha-MSH is also able to cross the blood-brain barrier (2).

Except for acetylation of the N-terminus and carboxy amidation in alpha-MSH, its structure is homologous with that of the N-tridecapeptide portion of adrenocorticotrophic hormone (ACTH) (2). The N- and C-Terminal portions of alpha-MSH are not essential for its bioactivity, therefore some modifications of the central portion of the protein lead to a chemical analogue that is 10- to 1000-times more potent than the natural hormone (1).

Afamelanotide, also known as melanotan, is a synthetic analogue of the naturally occurring melanocortin peptide hormone alpha-MSH. It is widely marketed via the internet to induce skin tanning by subcutaneous self administration.

Recently, synthetic Alpha-MSH-analogues like afamelanotide offered by online marketing are increasingly used as lifestyle drugs with the single intent to stimulate skin tanning.

CASE REPORT

A 30-year-old Caucasian patient presented to our outpatient clinic deeply tanned, but with patchy loss of pigmentation on his trunk and upper extremities (Fig. 1).

His medical history included atopic eczema in early childhood, the symptoms of which had gone into remission at the age of 5 years. His medical history was otherwise unremarkable.

At the age of 29 years he developed itchy eczematous lesions on his skin, which first appeared on his face, then progressively disseminated all over the skin. Topical steroids were used successfully.

At first consultation, multiple white macules measuring 1–2 cm in diameter, with minimal scaling were observed, mainly on the chest and upper extremities. The rest of his skin showed regular pigmentation suggestive of vitiligo. As additional side-effects, chronic fatigue, paresthesias, headache and nausea were reported.

Staining of a skin biopsy with haematoxylin revealed focal spongiosis, acanthosis and exocytosis of small lymphocytes. In the upper corium a perivascular lymphocytic infiltration with some eosinophilic granulocytes was noticed.

The skin biopsy was compatible with an eczematous dermatitis and did not support other differential diagnosis, such as tinea, mycosis fungoides, leprosy or vitiligo.

Fungal infection of the skin was excluded by mycological culture. Laboratory parameters, including serum-IgE levels, were within normal limits.

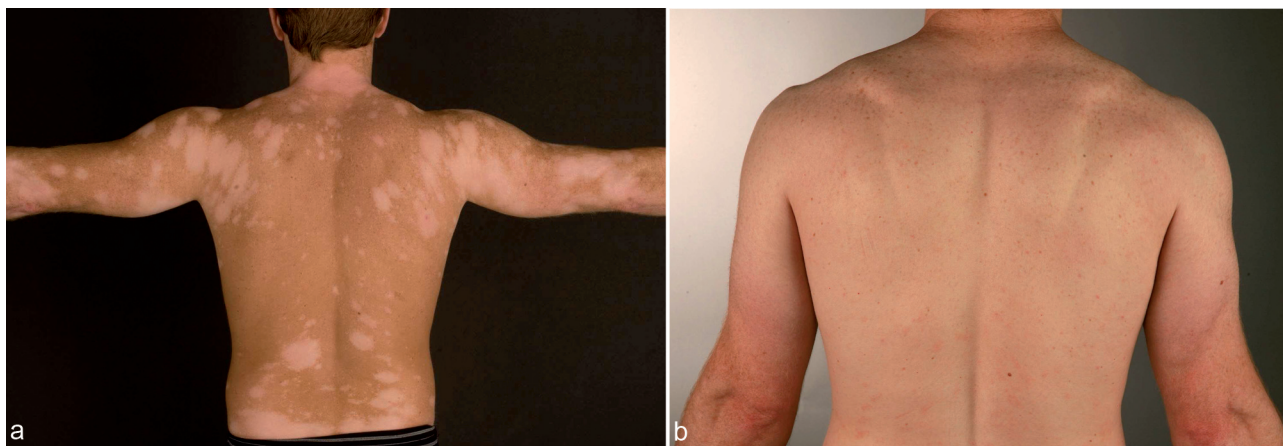


Fig. 1. (a) Development of white macules on the back. (b) Return to normal pigmentation after cessation of afamelanotide.

After several visits the patient admitted the use of afamelanotide injections. To achieve skin tanning the patient had self-injected several syringes of afamelanotide previously.

Within two months a total amount of 50 mg of melanotan had been injected.

Although the patient experienced headache, nausea and fatigue, he continued to use the drug, until he presented at our outpatient clinic.

Eight weeks after cessation of the afamelanotide injections, the pseudoleucoderma and the neurological symptoms had resolved.

DISCUSSION

Afamelanotide (Melanotan, CUV 1647) is a synthetically-produced peptide hormone which is able to imitate natural alpha-MSH. By immunoassay technique, alpha-MSH was found to have a plasma half-life of only 20 min in humans, whereas afamelanotide demonstrated a four-fold longer half-life (2).

Many cells of the human skin express melanocortin receptors, which are stimulated by the biologically active form of the precursor pro-melanocortin. The stimulation of these receptors is responsible not only for the pigmentation of the skin, but also for the regulation of lipogenesis via receptors on fat cells; furthermore, they play a role for growth by stimulation of receptors on chondrocytes. The anti-inflammatory effect of alpha-MSH is based on immunomodulatory and anti-fibrogenic processes of the skin cells, which are mediated by the MSH-receptors of dermal fibroblasts (3). In contrast, the stimulation of MSH-receptors on mast cells leads to a release of histamine and has a pro-inflammatory effect.

Damage to melanocytes by mediators and cellular components of the inflammatory reaction are thought to be responsible for the decreased ability of pigmentation of the eczematous skin. Furthermore, there is a mismatch in favour of CD4+ T cells. Activation of MHC-I-class peptide- sequence, presented by foreign

proteins with similarity to a melanocytic self-antigen, may lead to a diminished release of melanin (4, 5).

Internet traders take advantage of the induction of skin pigmentation by alpha-MSH analogue, by making it easily, but illegally, available via the internet.

Unregulated application of melanotan may confuse clinical presentation by promoting pre-existing melanocytic naevi. This could present an increased risk for melanoma development (6, 7).

There are several self-limited side-effects known, which are induced by the use of afamelanotide, including nausea, peripheral vasodilatation, fatigue, vomiting, gastrointestinal distress and headache. In this patient the above-mentioned side-effects disappeared a few weeks after stopping the melanotan injections.

This case demonstrates that alpha-MSH analogues should be added to the list of triggers of pseudoleucoderma.

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