Melanoma Associated with the Use of Melanotan-II

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Key Words
Melanoma · Melanotan-II · Skin pigmentation

Abstract

Background: Unlicensed use of melanotan-II (MT-II) to promote skin pigmentation has become prevalent amongst young people attending fitness centres. We present a case where the melanocyte stimulation of MT-II in combination with the use of sun tanning beds coincided with cutaneous melanoma.

Observation: A 20-year-old woman with Fitzpatrick skin type II was referred to a dermatology clinic. Clinical examination revealed a suspicious black melanocytic lesion in her left gluteal region. Furthermore, her skin was universally intensely pigmented. The melanocytic lesion was excised, and histology confirmed the diagnosis of melanoma. Three months prior to the excision the patient had conducted a 3- to 4-week course of self-injections with MT-II, intending an augmentation of sunbed tanning.

Conclusions and Relevance: This observation brings attention to the potential risks related to the use of the cyclic α-melanocyte-stimulating hormone analogue MT-II. There are several hazardous aspects of the possible widespread use of MT-II. As the drug is unlicensed and incompletely tested, the extent and types of adverse effects are unknown.

Clinicians are advised to be aware of the problem, and counsel their at-risk patients regarding the potential hazards related to the use of MT-II.

Introduction

Melanotan-II (MT-II) is an unlicensed synthetic analogue of the naturally occurring α-melanocyte-stimulating hormone (α-MSH), which is known to play a key role in human pigmentation via its agonistic effect on the melanocortin 1 receptor in melanocytes, and thus promoting intracellular synthesis of eumelanin in favour of pheomelanin which clinically is recognized as a ‘tan’. In the early 1980s a synthetic variant of α-MSH was developed. The substance [Nle4-D-Phe7]-α-MSH (4-norleucine, 7-D-phenylalanine-α-melanocyte-stimulating hormone) [1] was initially researched and reported as melanotan or melanotan-I (MT-I), and is now known under the generic name afamelanotide which is currently being tested for various dermatological diseases, e.g. vitiligo [2].

Afamelanotide is a linear α-MSH analogue. In contrast, MT-II is a newer shorter cyclic α-MSH analogue. MT-II seemed to have increased potency but with side effects such as penile erections and nausea [3, 4]. In a pilot phase I study, pigmentation was augmented after 5 subcutaneous doses given every other day [3]. Further studies have been conducted testing the drug in the treatment of erectile dysfunction, but to date the drug is unapproved outside clinical studies. The substance can illegally be obtained from the Internet or from gyms and sunbed parlours, without any medical control or restriction [5]. Several governmental drug-regulatory bodies have issued warnings [6] against the use of MT-II, and in the literature MT-II has been related to eruptive [7] and atypical naevi [8], melanoma [9], melanonychia [10] and rhabdomyolysis [11].

Report of a Case

A 20-year-old Caucasian woman, with Fitzpatrick skin type II, blue eyes and blond hair, was referred to a dermatology clinic for review of a changing pigmented lesion in her left gluteal region. The patient reported change in colour from light brown to jet-black with an associated sensation of tingling, following a 3-week course of MT-II conducted 3 months earlier. The patient presented a container labelled ‘Melanotan II 10 mg, sequence Ac-
**Fig. 1.** Haematoxylin and eosin stain showing pagetoid invasion.

**Fig. 2.** Haematoxylin and eosin stain showing pagetoid invasion. Atypical melanocytic cells marked with arrows.

**Fig. 3.** Immunohistochemical staining for melan-A. Atypical melanocytic cells seen as blue cells in epidermis.
Nle-Asp-His-D-Phe-Arg-Trp-Lys-NH₂, CAS No. 121062-08-6. She had injected herself with subcutaneous doses of 0.1 ml (1 mg) every other day for 3–4 weeks. She reported the regular use of sunbeds prior to and throughout her self-administration with MT-II. The patient described the effect as remarkable, resulting in a much darker tan as compared to the exclusive use of tanning beds. During the treatment the patient suffered from mild nausea. She had not been taking any other medication. There was no history of skin diseases and no family history of melanoma. Clinically her skin was universally intensely pigmented. In the left gluteal region a uniform black lesion was present. Dermoscopy revealed a pigmented skin lesion 4.5 mm in diameter, with a spitzoid pattern with a symmetrical but coarse pigment network, central blue-white veil and spike-like extensions at the periphery. The lesion was excised, and histology demonstrated a superficial spreading melanoma (Breslow thickness 0.32 mm, Clark level II). Atypical melanocytic cells with pagetoid invasion were present (fig. 1, 2). No ulceration was seen, and no mitoses were observed. Immunohistochemical staining (fig. 3) showed positive HMB45 and melan-A.

Clinical review 3 months later revealed multiple atypical naevi located especially on the trunk but no lesions suspicious for further melanoma.

Discussion

This observation brings attention to the potential risk of melanoma related to the use of the cyclic α-MSH analogue MT-II. The drug is unlicensed and incompletely tested, and the extent and types of adverse effects are unknown. Moreover MT-II is often used for merely cosmetic purposes by young people attending fitness studios.

The use of MT-II is often combined with the intense use of tanning beds, well established as a substantial risk factor for cutaneous melanoma [12].

In our case the close temporal relationship between MT-II injections and clinical growth and darkening of a melanoma points to a possible association.

The plausibility of a real causal association between MT-II and melanoma is however debatable. In vivo studies and studies in murine models have not shown any carcinogenic effect of the linear α-MSH analogue MT-I [4]. Investigations on the naturally occurring α-MSH have shown multiple functions of the hormone. On the one hand, studies have proven α-MSH to be anticarcinogenic with tumour suppressor effects, but on the other hand, research on melanoma cells in addition indicates a proinvasive effect of α-MSH, thus enabling the melanoma cells to evade immune surveillance [13]. When it comes to MT-II, however, the true biological potential of the substance remains unknown.

Physicians should be aware that MT-II has become a part of the tanning culture in certain subpopulations. Our observation indicates a possible association between MT-II and melanoma, but larger studies are needed to substantiate this linkage.

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Disclosure Statement

The authors declare no conflicts of interest.

References


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