



ACTAS Derma-Sifiliográficas

Full English text available at
www.elsevier.es/ad



CASES AND RESEARCH LETTERS

Eruptive Dysplastic Nevi Following Melanotan Use[☆]

Nevos displásicos eruptivos tras el consumo de Melanotan

Illegal use of Melanotan I and II has been reported and regulatory authorities have issued warnings in the United States and Europe.^{1,2}

Melanotan I and II are synthetic melanocortin analogs (α melanocyte-stimulating hormone) with greater potency and a longer half-life than endogenous α melanocyte-stimulating hormone. Melanotan I (afamelanotide) binds to the melanocortin I receptor (MC1R) to promote melanogenesis, both by proliferation of melanocytes and by regulation of tyrosinase activity. Melanotan II is less selective than its predecessor: it binds to MC2R, causing loss of appetite, and MC3R, initiating penile erections. This triple effect (tanning, loss of appetite, and increased sexual potency) has gained melanotan II the name “Barbie drug” and popularity among some sectors of the population.³ Melanotan II can be administered subcutaneously or as a nasal spray.

Currently in the experimental stage, Melanotan I (afamelanotide) is a promising option in dermatology. Ongoing phase I and II clinical trials are examining the prevention and treatment of erythropoietic protoporphyria, congenital erythropoietic porphyria, solar urticaria, and polymorphous light eruption, as well as the prevention of actinic keratosis and epidermal carcinoma in transplant recipients. The US Food and Drug Administration recently approved a phase II clinical trial of afamelanotide (SCENESSE, Clinuvel Pharmaceuticals Ltd) combined with narrowband UV-B therapy for the treatment of vitiligo.⁴

We report the case of a 25-year-old man who came to our department for the sudden eruption of multiple melanocytic nevi and rapid transformation of existing nevi. The changes occurred a few weeks after a 4-week course of subcutaneous Melanotan II. The patient (type II phototype) was a construction worker who regularly used a tanning bed. Examination revealed more than 100 melanocytic nevi, mainly on his back; many were clinically and dermatoscop-



Figure 1 Multiple melanocytic nevi, some of which are atypical, on the patient's back.

ically atypical (Figs. 1 and 2). We removed the 10 most atypical lesions, some of which were suspected of being melanoma. Histopathology revealed the lesions to be dysplastic melanocytic nevi; in 3 the dysplasia was severe (Fig. 3). A pigmented basal cell carcinoma on the right shoulder was also removed.

Other reports of illegal use of melanocortin analogs have appeared. Langan et al⁵ reported the first cases of transformation of preexisting nevi in 2 women (aged 30 and 48 years, phototype I/II) after they had used Melanotan I and II. Histopathology revealed benign melanocytic nevi and a severely dysplastic melanocytic nevus. Cardones

[☆] Please cite this article as: Hueso-Gabriel L, et al. Nevos displásicos eruptivos tras el consumo de Melanotan. Actas Dermosifiliogr. 2012;103:329-42.



Figure 2 Detail of an atypical lesion that was later removed.

and Grichnik⁶ subsequently reported the transformation of existing nevi and eruption of new melanocytic nevi with atypical clinical and histologic characteristics in a 40-year-old patient with a history of dysplastic nevi and melanoma. Cousen et al⁷ reported the case of a 19-year-old woman who was a regular user of a tanning bed and who developed eruptive nevi after she had used Melanotan II. Ellis et al⁸ reported a case of melanoma (Breslow depth of 1 mm) in a 23-year-old patient who consulted for an increase in size of a pigmented lesion on his leg after use of Melanotan I. The authors could not prove and did not suggest a causal relationship between the use of Melanotan I and development of melanoma. A second case of melanoma associated with this drug was recently reported by Paurobally et al,⁹ who described the transformation of an existing nevus on the abdomen of a 42-year-old woman 3 months after she had received Melanotan injections; histopathology revealed a 0.3-mm melanoma. Of note, all of these patients had the following risk factors: phototype I or II, multiple melanocytic nevi, personal and family history of melanoma, regular use of tanning beds, and repeated exposure to sunlight. It may be that patients with these factors are more likely to suffer onset and transformation of melanocytic nevi after taking Melanotan, with a potentially increased risk of developing melanoma.

Eruptive melanocytic nevi have been described in the literature in combination with certain bullous dermatoses and compromised immune status (in AIDS, in chemotherapy, and after transplantation).¹⁰ In all these cases, determining the potential risk of a new melanoma or transformation to melanoma is both difficult and open to debate. Nevertheless, close dermatoscopic and clinical monitoring is recommended in immunocompromised patients, and the most atypical lesions should be removed.

Easy access to these drugs on the Internet and their growing popularity will probably lead to reports of similar new cases. As dermatologists, we must suspect Melanotan use when faced with transformation of existing melanocytic nevi or the sudden eruption of new ones, especially in individuals with a suntan that is too intense for their skin type or for the time of year. The possibility that body dysmorphic dis-

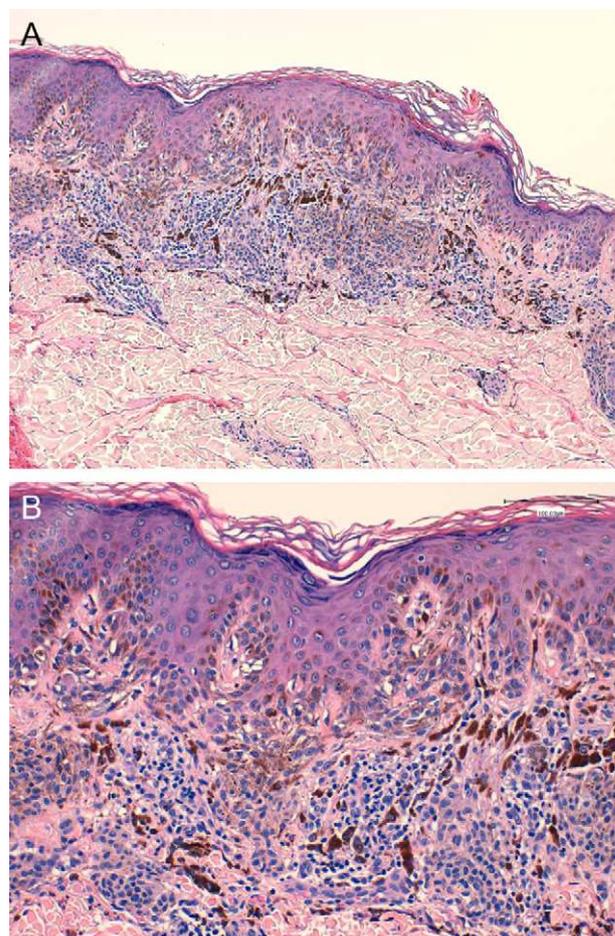


Figure 3 A, Proliferation of melanocytes at the dermoepidermal junction and in the dermis (hematoxylin-eosin, original magnification $\times 40$). B, Nests parallel to the skin surface; note their tendency to fuse. Focal cell atypia can be observed (hematoxylin-eosin, original magnification $\times 200$).

order (tanorexia) may also be present should be taken into account in some cases.¹¹

References

1. US Food and Drug Administration. FDA warns about unap-proved product, Melanotan II. 2007. Available at: www.fda.gov/consumer/updates/melanotan090507.html
2. Evans-Brown M, Dawson RT, Chandler M, McVeigh J. Use of Melanotan I and II in the general population. *BMJ*. 2009;338:b566.
3. Langan EA, Nie Z, Rhodes LE. Melanotropic peptides: more than just 'Barbie drugs' and 'sun-tan jabs'. *Br J Dermatol*. 2010;163:451-5.
4. Clinuvel Pharmaceuticals Ltd. Home page. Available at: <http://www.clinuvel.com>
5. Langan EA, Ramlogan D, Jamieson LA, Rhodes LE. Change in moles linked to use of unlicensed 'sun tan jab'. *BMJ*. 2009;338:b277.
6. Cardones AR, Greichnik JM. Melanocyte-stimulating hormone-induced eruptive nevi. *Arch Dermatol*. 2009;145:441-4.
7. Cousen P, Colver G, Helbling I. Eruptive melanocytic naevi following melanotan injection. *Br J Dermatol*. 2009;5:219-23.
8. Ellis R, Kirkham N, Seukeran D. Malignant melanoma in a user of melanotan I. *BMJ*. 2009. Rapid responses.

9. Paurobally D, Jason F, Dezfoulian B, Nikkels AF. Melanotan-associated melanoma. *Br J Dermatol.* 2011;164:1403-5.
10. Hueso L, Requena C, Serra-Guillen C, Alfaro A, Nagore E, Llobart B, et al. Nevos plantares múltiples posquimioterapia. *Actas Dermosifiliogr.* 2006;97:327-9.
11. Affleck A. Consider underlying body dysmorphic disorder in users of melanotan. *Br J Dermatol.* 2010;162:459-60.

L. Hueso-Gabriel,^{a,*} L. Mahiques Santos,^a L. Terrádez Mas,^b N. Santonja López^b

^a *Servicio de Dermatología, Hospital de Manises, Valencia, Spain*

^b *Servicio de Anatomía Patológica, Hospital de Manises, Valencia, Spain*

*Corresponding author.

E-mail address: luishueso@msn.com (L. Hueso-Gabriel).

doi:10.1016/j.adengl.2012.05.002

Fibrosing Cutaneous Sarcoidosis[☆]

Paniculitis sarcoidea fibrosante

To the Editor:

Subcutaneous sarcoidosis accounts for between 1.4% and 6% of skin lesions attributable to sarcoidosis, making it the least common subtype of specific lesion of this disease. It mainly affects white women in the fifth and sixth decades of life.¹ The lesions are typically firm, round or fusiform nodules with a diameter of between 0.5 and 2 cm; they are mainly found in varying numbers on the upper limbs and are usually bilateral and asymmetric.¹ Diagnosis requires histologic evidence of noncaseating granulomas in the subcutaneous tissue, without microorganisms.¹

We report the case of a 78-year-old woman with intrinsic asthma diagnosed 3 years earlier who developed subcutaneous sarcoidosis with marked fibroplasia. The patient had consulted for a mass that had appeared on her left forearm a year earlier, a similar mass on her right forearm, which had appeared a month later, and a third mass, which had appeared on her right elbow 3 months before consultation. Both she and her family commented that the size of the lesions had remained stable and that they were slightly tender. The only systemic symptom she reported was occasional joint pain in her upper limbs. Physical examination revealed 2 hard nodules, one on the left forearm and one in the right cubital region, measuring 2.5 and 5 cm respectively. They were not fixed to the deeper layers and there were no visible epidermal changes. A third, similar lesion, with a stony-hard consistency and also not adherent to the deeper layers, was observed on the right forearm (Fig. 1, A and B). Biopsy of the nodule on the right elbow showed a central area of sclerotic tissue with numerous sarcoid granulomas visible in the subcutaneous tissue (Figs. 2 and 3). Also visible was a discrete lymphocytic infiltrate. There were no foci of necrosis. An ultrasound scan of the right forearm showed a well-circumscribed, nonencapsulated, oval mass measuring 4.3 × 1.2 cm, with no muscle or bone involvement; the mass was slightly hyperechogenic and contained hypoechoic areas that gave it a mottled appearance. The chest scan showed hilar enlargement, which was confirmed on high-resolution computed tomography, which also revealed a reticulonodu-

lar infiltrate in both lungs. Spirometry showed an obstructive pattern, with a forced expiratory volume in the first second to forced vital capacity ratio of 66% of predicted. The electrocardiogram was normal and the Mantoux test was negative. Laboratory tests revealed an elevated creatinine level (2.08 mg/dL), an increased calcium to creatinine clearance ratio (0.64; normal range, 0.07-0.17 mg/dL), and decreased tubular reabsorption of phosphate (51%; normal range, 79%-89%). Serum levels of vitamin D, parathyroid hormone, calcium, phosphorus, and angiotensin-converting enzyme were within normal limits. No eye alterations were detected. Once the diagnosis of sarcoidosis was confirmed by clinical, histologic, and radiologic findings, the patient was started on prednisone, 30 mg once daily, for 6 weeks; the treatment resulted in a considerable improvement in the respiratory symptoms and a reduction in the size of the nodules.

Clinically, the nodules of subcutaneous sarcoidosis are rather nonspecific, although Pérez-Cejudo et al.² remarked that they could adopt an elongated form, but without forming cords as occurs in interstitial granulomatous dermatitis with arthritis.² Nevertheless, because of the nodular nature of the lesions, the differential diagnosis must include conditions associated with substance deposition, cysts, lipomas,

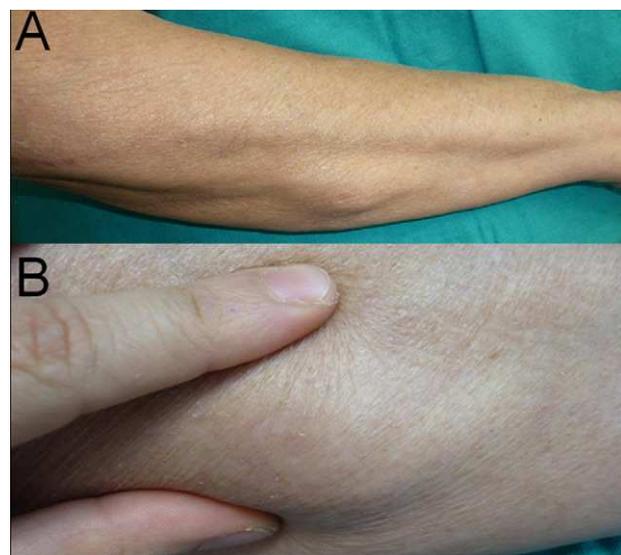


Figure 1 A, A firm, skin-colored nodule with well-circumscribed borders. B, Detail of the lesion showing an absence of epidermal changes.

[☆] Please cite this article as: Llamas-Velasco M, et al. Paniculitis sarcoidea fibrosante. *Actas Dermosifiliogr.*2012;103:331-3.