hypercellularity, nuclear atypia and frequent mitosis. The tumor was excised with a 3-cm margin. Histopathological examination of the resected specimen revealed a large, well-demarcated tumor mass, from the subpapillary dermis to the subcutaneous tissue (figure 1C). The tumor mostly consisted of densely proliferated spindle-shaped cells. The tumor cells showed significant cellular atypia with large, spindle-shaped, hyperchromatic nuclei with a few prominent nucleoli. Atypical mitotic figures were frequently seen. There were scant, capillary-like, diluted spaces in the tumor. Little extravasation of red blood cells was observed (figure 1D). In only a tiny part of the tumor, in the subpapillary dermis, the tumor cells showed vascular channel formation and the morphology of a conventional angiosarcoma (figure 1E). To confirm the endothelial origin of the tumor cells and exclude sarcomas other than angiosarcoma, immunohistochemical staining was done. The tumor cells stained positive for vimentin, α-smooth muscle actin (SMA;1A4), CD99, Bcl-2, CD31, CD34, D2-40, Fli-1, ERG and INI-1, and negative for AE1/AE3, S-100, MelanA, CD68, factor VIII-related antigen, Ulex europaeus agglutinin 1 lectin (UA-1), c-myc and HHV8 latency-associated nuclear antigen (LANA-1) (figures 1F-O).

From these clinical and histopathological features, we diagnosed the tumor as spindle cell angiosarcoma. The patient and her family declined postoperative adjuvant therapy. For the 2 years since the operation, neither local recurrence nor metastasis has been identified.

Angiosarcoma shows several rare variants: a spindle cell variant, a granular cell variant [3], a foamy cell variant [4] and a signet ring cell variant [5]. Granular cell angiosarcoma consists predominantly of cells with abundant granular cytoplasm that stain positively with markers for lysosome (CD68, NCK1/C3) [3]. Foamy cell angiosarcoma is made up of cells with abundant vacuolated cytoplasm and resembling foamy histiocytes [4]. Signet ring cell angiosarcoma is a subtype of epithelioid angiosarcoma that is characterized by predominant signet ring cells [5].

Spindle cell angiosarcoma, which we experienced, is an extremely rare variant of angiosarcoma and, to date, only a small number of cases have been reported [1, 2]. It is very difficult to make the diagnosis only by histopathological features [2]. Especially in our case, it was very difficult to make the definite diagnosis because the tumor cells showed vascular differentiation only focally at the superficial margin of the tumor. Thus, we needed to perform immunohistochemical staining on the tumor cells with several antibodies. In addition to CD31 and CD34, Fli-1 has been shown to be fairly specific to endothelial cells [6]. ERG differentiates cutaneous angiosarcoma from histological mimics [7]. Thus, in the present case, the positive staining for CD31, CD34, D2-40, Fli-1 and ERG on the tumor cells strongly supported the diagnosis of spindle cell angiosarcoma. High-level amplification of myc was found in 55% of angiosarcoma secondary to irradiation or chronic lymphedema but primary angiosarcoma lesions, as in the present case, are known to be negative for c-myc [8]. In addition, negative staining for HHV8 LANA-1 [9] excluded Kaposi’s sarcoma in the present case. In this case, we ruled out epithelioid sarcoma by negativity for AE1/AE3 and positivity for INI1. Negativity for INI1 can be used to confirm the diagnosis of epithelioid sarcoma [10].

In conclusion, this case suggests that we should keep spindle cell angiosarcoma in mind as a differential diagnosis for spindle cell tumors, particularly for those on the scalp of the elderly.

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Eruptive naevi and darkening of pre-existing naevi 24 h after a single mono-dose injection of melanotan II

A 24-year-old male bodybuilder reported the eruption of multiple new naevi and darkening of pre-existing naevi 24 h after a single subcutaneous injection of illegally acquired melanotan II. Additionally, he described a tanning effect on the whole skin. The patient usually used sunbeds at least once every 4 weeks.
The blond and blue-eyed man presented with a bronzed skin and more than 100 moles, especially on the trunk and the face, different in size and colour (figure 1A). Dermatoscopically, we saw both symmetric and asymmetric moles, with distinct and fading borders of brown, dark brown and black net structures, as well as irregularly distributed dark brown and black dots and bizarre pigmented patterns with accentuated pigmentation in the periphery of lesions (figures 1D-F).

Histopathological evaluation of one very prominent naevus revealed a symmetrical melanocytic lesion with aggregations of monomorphic, strongly pigmented melanocytes at the dermal-epidermal junction, but no signs of malignancy (figures 1B-C).

We discussed the unknown effects of melanotan II with the patient, expressed a serious warning about its further use and advised regular examinations of the skin to screen for possible malignant changes. Unfortunately, the patient did not return for the scheduled follow-up visits.

Melanotan I and II were developed to stimulate the body’s natural pigmentary system prior to sun exposure, as a protection against UV-related pathological skin conditions, such as erythropoietic protoporphyria and polymorphic light eruption [1]. Both substances are synthetic analogues of the alpha-melanocyte-stimulating-hormone (α-MSH), leading to increased eumelanin formation. Melanotan I (afamelanotide) is composed of 13 amino acids and is 100-fold more effective in tanning than α-MSH [1]. Currently, it is being tested in several clinical studies for different indications, including erythropoietic protoporphyria, polymorphic light eruption, vitiligo and skin cancer prevention in organ transplant recipients [2].

Melanotan I is licensed as an orphan drug for solar urticaria and erythropoietic protoporphyria [2]. Its safety and effectiveness have been evaluated in more than 620 patients. Melanotan II, consisting of 7 amino acids, in addition to a tanning effect, as shown in a small study with 3 male patients, may be associated with spontaneous penile erections and a desire to stretch and yawn [1]. Further side effects include nausea, vomiting, hypertension and darkening of pre-existing moles, as reported in web forums and newspapers (www.melanotan.org). Rapid pigmentation of pre-existing naevi and eruptive naevi following melanotan II injections have also been reported, even in a teenage patient with FAMMM syndrome [3-6]. Furthermore, development of melanoma in situ and malignant melanoma after self-administration of melanotan I or II has been reported [7-9]. But to the best of the authors’ knowledge, eruption of naevi has never been observed as fast as within 24h after a single injection of melanotan II, as in our case. The patient frequently used tanning beds, therefore a synergistic effect of UV-radiation and melanotan II on pigmentation is not excluded. But we strongly believe the mole eruption to have been mainly caused by melanotan II because it was very sudden and caused the patient to present to the dermatologist.

No official data on safety or effectiveness of melanotan II are available from clinical studies. It has widespread illegal use as an aphrodisiac, fat-burning substance and tanning pill, provided through the internet. The different available products are often collectively called “melanotans” without differentiating between melanotan I and II.

Several national and international official medical authorities, including FDA, MHRA and EMEA, sent out warnings on the use of melanotan II. There is not yet any estimate on the risk of cardiovascular disease or melanoma. Additionally, users risk infections, including blood-borne viruses, by needle sharing.

Recently, Nelson et al. reported systemic toxicity and rhabdomyolysis after a high dose of subcutaneous melanotan II [10]. Our report illustrates the enormous effect on melanocytes after just one injection of melanotan II. The drug is not licensed and serious side-effects, including malignant melanoma induction, are harmful risks to be warned about. While melanotan I is under investigation for epithelial cancer prevention in organ-transplant recipients, melanotan II seems less suitable because of its side effects. But there are also reports of the development of melanoma under treatment with melanotan I [8] and even under α-MSH, so that this indication needs to be further investigated and patients carefully observed.