Correspondence and Opinions

December 6, 2003.

Case 2
A 41-year-old woman, without a notable history, was treated with localized PUVA therapy for multiple plaques of tinea capitis. The dose of 8-MOP was 0.6 mg/kg, i.e. 4 tablets 2 h before irradiation. The sessions took place at 4 p.m., 3 times a week (Monday, Wednesday and Friday). Six weeks after the start of treatment, the patient complained of sleep disorders punctuated by the ingestion of 8-MOP. She had problems in falling asleep and also when sleeping, and was frequently awakened during the night. These disorders appeared regularly on the day after ingestion of 8-MOP, i.e. either on Tuesday, Thursday or Saturday. They improved on the days of the sessions and stopped completely from Sunday to Monday. Insomnia disappeared during a 1-week phototherapy-free period and recurred when treatment was re-introduced. Reduction in the dose of 8-MOP to 3 and subsequently 2 tablets per session did not lead to any improvement. Finally, when the frequency of the sessions was reduced to twice weekly, the symptoms improved, and it was possible to continue PUVA therapy. An isoniazide acetylation test in this patient revealed a slowly acetylating phenotype [2].

Our cases have the following points in common: the sleep problems were punctuated by ingestion of 8-MOP, re-introduction of psoralen after a treatment-free period of 2 and 1 weeks, respectively, provoked recurrence of insomnia and, finally, these side-effects only disappeared when treatment was withdrawn. The existence of such side-effects is probably the result of a multi-factor event, in which the pharmacological activity of psoralens plays an essential role. Psoralens or furocoumarins are natural or synthetic substances derived from coumarin. The latter are used in dermatological therapeutics because of their photosensitizing nature and capacity to inhibit cell proliferation in combination with UVA irradiation. PUVA therapy also exhibits photopigmentogenic potential by increasing the number of functional melanocytes and by stimulating melanogenesis. This effect results from the activation of tyrosine hydroxylase, a key enzyme in melanogenesis, which induces the production of eumelanin and phaeomelanin. By stimulating this enzyme, the combination of psoralen and UVA would enhance the dopamine and noradrenaline route of synthesis and, consequently, increase these psychostimulating neuromediators. Moreover, noradrenaline would play an important role in the pineal secretion of melatonin, the neuromediator of sleep that regulates circadian rhythms [3]. Through this noradrenergic stimulation, PUVA therapy might modify the normal cycle of melatonin secretion, and hence explain why certain patients exhibit sleep disorders during treatment. Furthermore, it has been established that ingestion of psoralen is followed by a significant increase in melatonin plasma levels [4]. Lastly, synthesis of melatonin results from serotonin acetylation under the effect of serotonin-N-acetyltransferase. The activity of this enzyme follows a circadian rhythm and increases greatly during the night. The existence of a slowly acetylation phenotype in our second case may also affect the melatonin route of synthesis, enhancing the accumulation of serotonin.

In these 2 cases it was the spontaneous, precise and almost simultaneous description of sleep disorders made by both of our patients that attracted our attention. Although this side-effect is only clinically manifest in a few probably predisposed patients, it should be known to the physicians in order to limit the diagnostic dithering it may generate.

References

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Important Announcement

Board Certification in Dermatopathology

The International Board of Dermatopathology will organize under the auspices of the International Committee for Dermatopathology the first Certifying Examination in Dermatopathology (Diploma in Dermatopathology) in Frankfurt/Main, Germany, on December 6, 2003.

Participating Societies:
International Society of Dermatopathology
European Society for Dermatopathology
Ibero-Latin American Society of Dermatopathology

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