

Flutamide photosensitivity – residual vitiliginous lesions

J. VILAPLANA, C. ROMAGUERA, A. AZÓN AND M. LECHA

Servei de Dermatologia, Hospital Clínic i Provincial, Facultat de Medicina, Universitat de Barcelona, Spain

A case of flutamide photosensitivity is reported in a patient receiving treatment for prostate cancer. Photopatch testing with flutamide at 10 and 20% in acetone was positive and controls negative. Other reports in the literature indicate that flutamide photosensitivity can be produced either by UV-A or UV-B, but the small number of reports and the differences in the tests performed do not allow the specific characteristics of flutamide photosensitivity to be established. Presently it would be advisable, due to the frequent use of this drug, to include flutamide in the investigation of photosensitive patients.

Key words: photosensitivity; flutamide; vitiligo; photopatch testing; UV-B; UV-A; medicaments.
© Munksgaard, 1998.

Accepted for publication 22 September 1997

Flutamide is a potent non-steroidal antiandrogen, which acts by inhibiting the conjugation of androgens to their tissue receptors. The pharmacological data about the drug indicate a potential photosensitivity reaction, with erythema and vesiculo-erosive necrolytic lesions. However, published reports of this type of reaction are rare, considering the frequent use of the drug in the treatment of prostate cancer.

Case Report

A 67-year-old man had been working as gardener. Prostate cancer was diagnosed in January 1996. He

was unwilling to undergo surgical treatment, and Eulexin® (flutamide) 750 mg daily, Procrin® (leuporeline) 0.2 ml s.c. 2× daily and radiotherapy were therefore exhibited. On 8 May 1996, he consulted a dermatologist with erythema, vesicular lesions and pruritus on exposed skin. The clinical diagnosis was drug-induced photosensitive eczema. Medication was withdrawn and he was treated with topical corticosteroids and oral antihistamines. Lesions cleared after 10 days. On 26 July, he re-attended with vitiliginous lesions on previously affected skin (Fig. 1). Treatment with Difur (Calaguala) 1 tablet 3× daily, phenylalanine 10% gel and topical corticosteroids was started



Fig. 1. Vitiliginous lesions initially.



Fig. 2. Vitiliginous lesions 9 months later.

Table 1. Photopatch test results with UV-A

	Irradiated (D1)		Non-irradiated	
	Results		D2	D4
	D2	D4		
flutamide 10% acet.	+	++	–	–
flutamide 20% acet.	++	+++	–	–
leuproreline 10% alc.	–	–	–	–
leuproreline 20% alc.	–	–	–	–

Table 2. Photopatch test results with UV-B

	Irradiated (D1)		Non-irradiated	
	Results		D2	D4
	D2	D4		
flutamide 10% acet.	+	+	–	–
flutamide 20% acet.	+	++	–	–
leuproreline 10% alc.	–	–	–	–
leuproreline 20% alc.	–	–	–	–

and the patient was referred for phototesting. Vitiliginous lesions have slowly been shrinking in size with treatment, and 9 months after their appearance, they are 50% smaller (Fig. 2).

On 16 September, 4 months after stopping medication, monochromator testing revealed no abnormal results and MED for 280, 307 and 320 nm performed on the skin of mid-upper back was within normal range (>50 mJ/cm² for the wavelengths tested) (Oriel Co. Monochromator Mod. 66023; Stratford, USA). Photopatch testing (UV-A source – Philips HPA 2000 – dose 15 J/cm² – irradiation D1) with the GEIDC standard series was negative. Photopatch tests with flutamide 10% and 20% acet. were positive at D2 and D4 and negative with leuproreline 10% and 20% alc. (Table 1). Photopatch testing was repeated with UV-B (UV-B source – Philips TI20/12RS – dose 25 mJ/cm² – irradiation D1) also showing positive results for flutamide 10% and 20% acet. and negative for leuproreline 10% and 20% alc. (Table 2). 10 controls with identically-performed photopatch tests were negative for both drugs and both doses of UV-A and UV-B radiation used were suberythematous for the normal population.

Discussion

Since the introduction of flutamide in the treatment of prostate cancer, this drug has been used

with increasing frequency. 5 cases of cutaneous photosensitivity have so far been published (1–4). All reported patients developed eczematous lesions on exposed areas, associated with pruritus or a burning sensation. The lesions disappeared quickly after withdrawing flutamide and reappeared if the patient was rechallenged with the drug, confirming that flutamide was the cause (4). Our patient initially showed the same type of eczematous eruption as reported in other cases, but developed vitiliginous patches after remission of these lesions.

Phototesting in the previous reports has been performed with different methodologies, especially photopatch testing. UV-B and UV-A MED values appear to have been within the normal range in all cases. Tests were always performed after remission of the lesions and stopping the medication. Only the patient reported by Leroy et al. (4) showed lowered MED values during treatment and normalization of MED values when no medication was administered. The results of phototesting in our patient are therefore in agreement with the results of the majority of previous reports where phototesting has been performed after stopping the medication. It must be admitted that, in the present case, phototesting was performed only with wavelengths within the UV-B range. However, UV-A irradiation during photopatch testing may also be considered a proof of absence of abnormal responses to UV-A.

Discrepancy between the results of phototesting and photopatch testing should take into account that the patients (present case and previous reports except for the Leroy et al. case) were tested after variable periods of stopping medication. This may modify the outcome of phototests but not necessarily photopatch tests, where the offending drug is applied on the skin in much higher concentrations than those resulting from oral intake. There have been differences in the concentrations of the drug used for photopatch testing. This may also have been the cause of discrepancies in the results. In our opinion, the optimum concentration seems to be 20%, which gives positive results with UV-B and UV-A (1, present case). Although photopatch testing is not a reliable test for systemic drug photosensitization (4), 3 of the published reports found positive results, 4/6 cases with UV-A (1–3, present report) and 2/6 with UV-B (1, present report). These results are difficult to reconcile with the reported absorption spectrum of flutamide (1) of 292 nm. If we take together all the results obtained in different reports, it seems reasonable to consider that flutamide sensitizes to both UV-B and UV-A. As a supplementary argument in favor of the relevance of the photopatch test results, we have

tested 10 normal subjects as controls and obtained negative results.

References

1. Miraillon I, Jeanmougin M, Manciet J R, Revuz J, Bagot M. Photoallergic reaction induced by flutamide. *Photodermatol Photoimmunol Photomed* 1991; 8: 264–265.
2. Fujimoto M, Kikuchi K, Imakado S, Furue M. Photosensitive dermatitis induced by flutamide. *Br J Dermatol* 1996; 135: 496–497.
3. Zabala R, Gardezabal J, Manzano D, Aguirre A, Zubizar-

reta J, Tuneu A, Diaz Pérez J. Fotosensibilidad por flutamida. *Actas Dermosifiliogr* 1995; 86: 323–325.

4. Leroy D, Domp Martin A, Szczurko C. Flutamide photosensitivity. *Photodermatol Photoimmunol Photomed* 1996; 12: 216–218.

Address:

J. Vilaplana
Servei de Dermatologia
Hospital Clinic
Villarroel 170
08036 Barcelona
Spain