

LETTER TO THE EDITOR

Photosensitivity associated with systemic triflusal therapy

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To the Editor,

Triflusal (2-acetyloxy-4-trifluoromethylbenzoic acid) is a fluorinated acetylsalicylic acid analogue used as an antiplatelet drug for prophylaxis of thromboembolic disease. Its main side effects are those concerning the gastrointestinal system. We report a systemic photosensitivity and a solar urticaria in a patient under triflusal therapy.

A 72-year-old man, with Fitzpatrick skin phototype II and medical history of hypertension undergoing treatment with olmesartan since 2005, was diagnosed with a carotid stenosis in September 2011; therefore, triflusal (300 mg/12 h) was prescribed. Two years later, he was sent to our Photobiology Unit because of outbreaks of eczematous lesions involving the photoexposed areas of his face, neck and hands (Fig. 1a). Those lesions had appeared 1 month after the introduction of triflusal, and persisted despite the use of topical corticosteroids and oral antihistamines. He was taking no other medication. In order to rule out a systemic photosensitivity, phototesting was performed on the skin of his lower

back, using a solar simulator to test UVB and UVA (Xenon arc 16S; Solar Light Co., Philadelphia, PA, USA) and a slide projector to test visible light (GAF 502 Autofocus slide projector lamp). The doses we used were from 3.7 to 24.7 mJ/cm² for UVB and from 0.5 to 10 J/cm² for UVA. An urticarial reaction was observed 15 min after UVB irradiation (>3.7 mJ/cm²) (Fig. 1b) and UVA irradiation (>0.5 J/cm²) (Fig. 1c), whereas visible light showed a negative response. These lesions were highly pruritic and cleared after 30 min. Moreover, the minimal erythema dose to UVB (UVB-MED) was 10 mJ/cm² (normal value 28 ± 4 mJ/cm², pathologic value <19 mJ/cm²) (1) and response to UVA was abnormal (erythema after a single dose of 10 J/cm²) (Fig. 1d). He was asked to discontinue triflusal, which was replaced by acetylsalicylic acid (ASA), with a subsequent improvement of his lesions. One week after this switch, the patient was almost asymptomatic, the UVB-MED had risen to 13.5 mJ/cm² and there was no urticarial response to UVA (up to 10 J/cm²). A new phototest was performed 2 months later, showing a negative response to UVA and a UVB-MED of 24.7 mJ/cm² (an increase above 70% of the previous one). Photopatch tests were also performed with the baseline series of the Spanish Group of Photobiology (MartíTor, Barcelona, Spain) being applied in duplicate to the skin of the upper back, extended with triflusal, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB, the triflusal active metabolite) and ASA. All of them were prepared by the hospital pharmacy at 1% in petrolatum and were applied in triplicate to the skin of the upper back. After 2 days, one set was removed and irradiated with 5 J/cm² UVA, and the set of triflusal, HTB and ASA was also removed and irradiated with a sub-UVB-MED dose (17.3 mJ/cm²). Readings were done immediately, at 30 min, 60 min, days 1, 2 and 3 postirradiation. Immediate reading was negative, whereas a palpable erythematous-edematous reaction was observed at day 1 postirradiation only in triflusal and HTB UVB photopatches. A weak non-palpable erythema was also noticed in the same patches irradiated with UVA (Fig. 2). Laboratory tests were also performed in

order to rule out lupus and porphyria, being negative or within the normal range.

Systemic photosensitivity associated with triflusal was first described in 1987 by Serrano *et al.* They performed photopatch test in six healthy volunteers demonstrating no abnormal reaction to UVB or UVA in any of them (2). Two additional cases have been reported afterwards, both with photopatch tests suggesting a photoallergic drug reaction (3, 4). In our case, such as in the previous ones, both triflusal and its active metabolite displayed a positive response with both UVA and UVB, whereas ASA did not. This fact supports the idea that trifluoromethyl group is essential in the photosensitizing ability. The maximum action spectrum of triflusal appears to be in the UVB range, unlike most photosensitivity reactions, which are typically associated with UVA wavelength. Although rare, this response has been previously reported with other drugs like griseofulvin and diphenhydramine (4).

On the other hand, solar urticaria is an uncommon photodermatoses characterized by urticarial lesions induced by UV, visible light or both. It may occur spontaneously or be secondary to exogenous agents. Drug-induced solar urticaria is a very unusual condition and only sporadic cases have been reported in individuals exposed to tar and pitch (5) and related to chlorpromazine (6, 7) benoxaprofen (8), repirinast (9) and tetracycline (10). In our patient, photoprovocation was achieved with both UVB and UVA but not with visible light, as described with other drugs.

In conclusion, we report a patient who was diagnosed with urticaria and a photosensitivity reaction associated with oral triflusal. The lack of symptoms and phototest normalization after drug withdrawal, coupled with the photopatch test results, support this diagnosis. A number of phototoxic drugs have been reported to have immediate (urticaria) and delayed erythema patterns of response, benoxaprofen and the systemic PDT agents as an example. Although it is

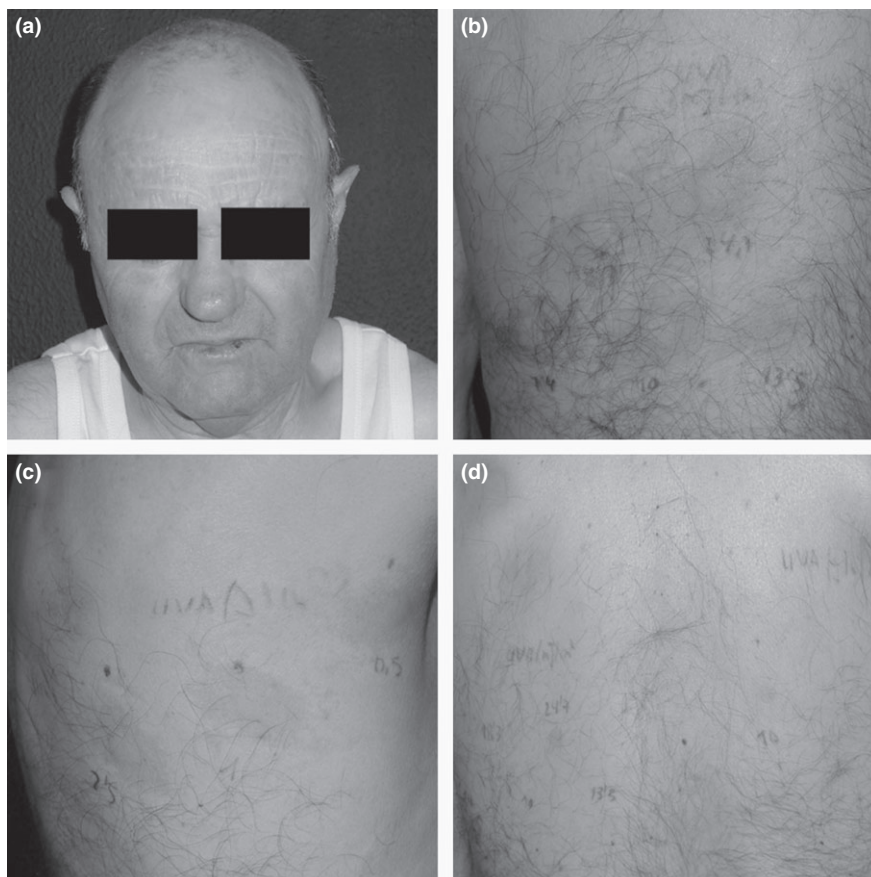


Fig. 1. (a) Erythema with slight desquamation on the forehead, cheeks and nasal dorsum and superficial erosions on the lower lip. Urticarial lesions 15 min after UVB (b) and UVA (c) irradiation. (d) Phototest: UVB-MED: 10 mJ/cm² and abnormal response to UVA (erythema with 10 J/cm²).

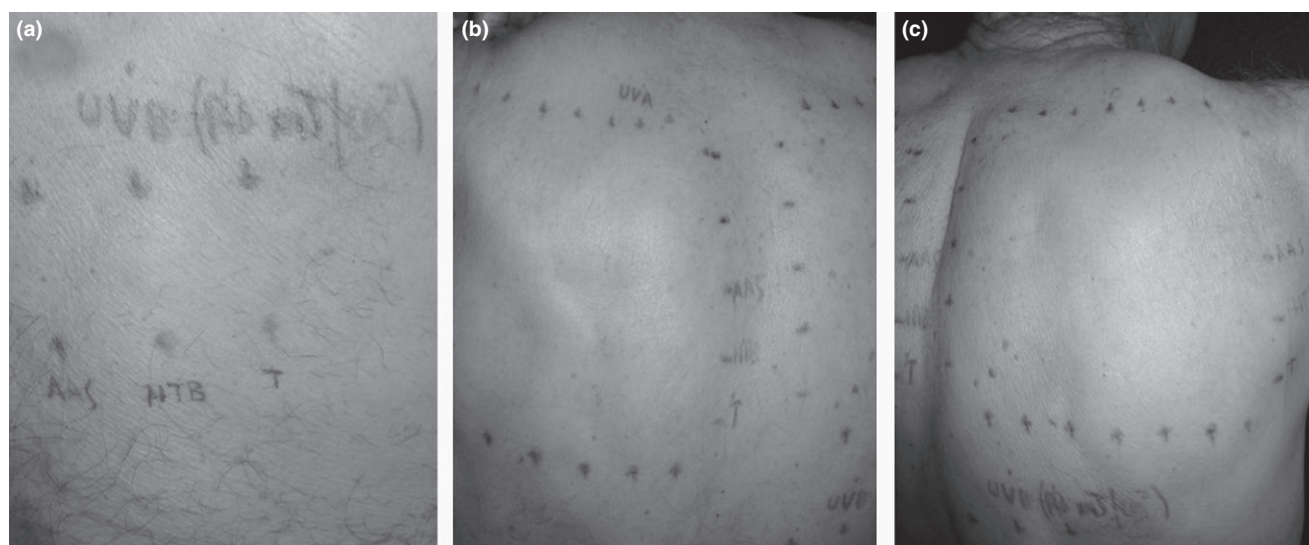


Fig. 2. Photopatch test. (a) Palpable erythematous-edematous reaction at 24 h postirradiation in triflusal and HTB UVB photopatches. (b) Weak non-palpable erythema in the same products irradiated with UVA. (c) Negative response in the non-irradiated set.

considered an underdiagnosed disease, only three cases of photosensitivity and none of solar urticaria associated with triflusal have been reported to date. Since triflusal is a drug commonly used in our country, we consider that its photosensitizing potential should be taken into account.

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