Table 1 Provocation cumulative dose, variation of total nasal resistance during the follow-up times, and symptoms in patient undergone metamizole challenge test

	Metamizole
Cumulative dose (mg)	10
R T0 (±%)	0.25
R T1 (±%)	0.55 (+120)
Symptoms	Rhinitis and conjunctivitis
Latency after the first dose (minutes)	30

R T0, nasal resistance at baseline; *R* T1, nasal resistance after the first dose.

mechanism is only partially known. Himly et al. (7) developed a novel *in vitro* system to detect allergen-specific IgE that revealed an IgE-mediated mechanism in patients with adverse reactions to pyrazolones, mainly cutaneous manifestations with asthma or asthma plus rhinitis. In our patient, the negative responses to skin tests in the presence of naso-ocular symptoms and increase in $R = +120$ on ARM indicate that a metamizole metabolite may induce the IgE-mediated reaction. This hypothesis fits well with the rapidity of the onset of reaction after metamizole intake (30 min), the absence of asthma (usually present in patients who reacted to blocker of cyclooxygenase-1 agents), and tolerability to aspirin.

Asero et al. (8) showed that in patients with urticaria following a single NSAID (other than aspirin), the OCT with aspirin is safe and discriminates between single and multiple reactors according to the tolerance to aspirin or not. Here, because of the negative response to aspirin, it could be argued that not only in cases of urticaria but also in those with respiratory reactions to a single NSAID, the provocation test using aspirin could be used to identify naso-ocular responders to one or multiple NSAIDs. The pyrazolones are drugs that may cause multiform reactions with allergic, nonallergic, or mixed hypersensitivity which warrant further studies.

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Systemic photoallergy to terbinafine

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Keywords: adverse drug reactions; photoallergy; photoallergic dermatitis; photopatch testing; terbinafine.

Terbinafine is an allylamine antimycotic drug with a relatively good safety profile. Minor skin rashes have been observed in 2% of treated patients (1). Photosensitivity because of terbinafine seems very rare: Until now, only isolated cases of terbinafine-induced lupus erythematosus (LE), subacute cutaneous LE or terbinafine-exacerbated LE have been reported (2–4). To the author's knowledge, this is the first description of photoallergic dermatitis to this drug.

This is the first report of photoallergic dermatitis to terbinafine.

A 60-year-old man was prescribed oral terbinafine (TerbiGen™, Merck Generics, Potters Bar, UK) for his onychomycosis. The treatment started in a sunny September, with the patient spending daily 1–3 h outdoors. On day 6 of the therapy, an itching skin rash emerged on his forehead and dorsi of hands and gradually aggravated. Suspecting a connection with the newly started antimycotic, the patient discontinued TerbiGen™ on day 8. However, erythema, oedema and scaling continued to progress on his face, décolleté and dorsal neck, accompanied by moderate malaise and slightly elevated body temperature. Covered areas of the skin were not involved. On day 12, the patient sought medical help after orbital swelling appeared in the preceding night. Local and oral steroids led to a significant improvement overnight, and complete clearance within 2 days.

Suspecting a photoallergic reaction, photopatch tests were carried out 2 months later with an extensive series

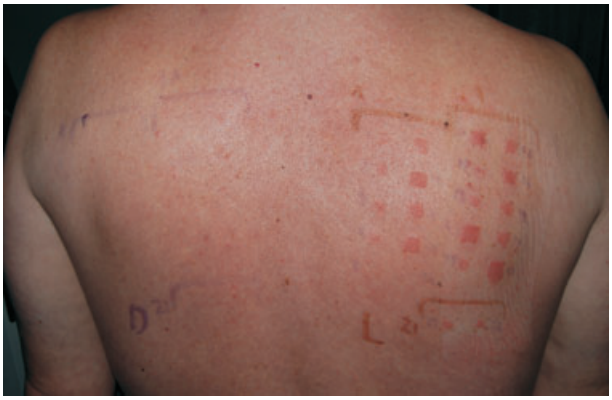

Figure 1 Photopatch testing with a dilution series (1–25%) of terbinafine hydrochloride, dissolved in liquid paraffin, water and ethanol, 96 h after application of the tests and 48 h after irradiation with 5 J/cm^2 UVA. On the left-hand side (nonirradiated), no reaction to the same set of test substances.

of photohaptens (cosmetics, sunscreens, drugs, etc.), including patient's own drugs taken during the episode: terbinafine, thiamazole, perindopril and bisoprolol (tablets crushed and mixed with 0.5 ml saline 0.9%), following standard methodology (5). The only positive reaction was to TerbiGen^{TM}, scored as ICDRG "+" after 72 h of application to the skin (24 h after irradiation of the site with 5 J/cm^2 UVA) and "++" after 96 h (48 h after irradiation). Crushed tablet seemed useful for initial testing; however, the results needed to be confirmed with pure substance. Thus, a second round of photopatch tests was undertaken with a dilution series of pure terbinafine hydrochloride (Sigma-Aldrich, Steinheim, Germany) dissolved in liquid paraffin, ethanol and water at 1, 2, 5, 10 and 25% – all with "+" to "++" reactions. All tests remained negative on the nonirradiated side (Fig. 1). To exclude false-positive (phototoxic) reactions, the author underwent the same tests – all with negative results. Later on, five other patients with suspected photoallergy tested negative with terbinafine at 1% and 5%. Paraffin proved better vehicle for the hydrophobic terbinafine, than ethanol or water. Based on the present case, photopatch testing with 1% and 5% terbinafine hydrochloride in paraffin seems most advisable until collecting more experience.

The fact that the symptoms continued to aggravate after cessation of the exposure, along with negative test results in six controls, suggested a photoallergic, rather than phototoxic reaction. However, the relatively short period between starting terbinafine therapy and developing symptoms seemed somewhat confusing, as contact allergy requires an induction phase to develop and does not appear upon first encounter with the offending photohapten. Moreover, the induction of contact allergy seems to require exposure to the hapten via the skin to "condition" effector lymphocytes to migrate to the skin as target organ (6), which seems also true for photoallergy. After repeated inquiries, the patient remembered that several years prior to the present episode, he was prescribed Lamisilatt^{TM} cream (terbinafine hydrochloride 1%) for some rash on his hands. He could recall that he had used the cream for 1–2 weeks and this was in the summer. It seems that this combination of a pre-existing inflammatory skin condition (disrupted skin barrier, danger signals) with exposure to terbinafine and solar irradiation might have created circumstances (formation of photoadducts) leading to the induction of his photoallergy.

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