

Vulvovaginal allergic contact dermatitis from nifuratel: report of a case and review of the literature

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Nifuratel (*N*-(5-nitro-2-furfurilidene)-3-amino-5-methyl-mercaptomethyl-2-oxazolidine, CAS 4936-47-4) has antimycotic, trichomonacidal, and antibacterial properties. It is used as an ingredient in topical medicaments for the treatment of vulvovaginal infections (1).

Case Report

A 40-year-old non-atopic woman presented with a severe, partly erosive vulvitis, and vaginitis. Additionally, she showed a symmetrically distributed haemorrhagic erythema and induration on the inner thighs. She was unable to walk because of severe pain and thus admitted to the hospital. She reported that she had used Inimur[®] vaginal suppositories [ingredients: nifuratel, corn starch, lactose, polyethylene glycol 6000 (macrogol), tartaric acid, sodium hydrogen carbonate, and magnesium stearate] and Inimur Myko[®] vaginal cream [ingredients: ciclopiroxolamine, octyldode-

canol, liquid paraffin, stearyl alcohol, cetyl alcohol, tetradecan-1-ol, *N,N*-bis (2-hydroxyethyl) coconut fatty acid amide, polysorbate 60, sorbitan stearate, and lactic acid] for 8 days for the treatment of a fungal vaginitis. The medicaments had been applied using latex gloves. Bacterial and mycotic cultures were negative. Her antimycotic therapy was immediately stopped. Treatment with a glucocorticosteroid cream was started, which resulted in a complete healing of the contact dermatitis.

Patch testing of Inimur[®] vaginal suppositories revealed a positive reaction (according to the criteria of the International Contact Dermatitis Research Group on D2 and D3 readings, respectively). Patch testing (including the standard and additional series of the German Contact Dermatitis Research Group, the other patient's own products and latex) was otherwise negative with exception of nickel sulfate. Patch testing of the ingredients was planned, but could not be performed as the patient refused a 2nd patch test procedure.

Discussion

Although we were not able to perform a patch test of the ingredients of Inimur[®] vaginal suppositories, we believe that nifuratel had caused the allergic contact dermatitis (ACD) in our patient as the other (commonly used) ingredients are not known contact allergens. Only 6 cases of ACD to nifuratel have yet been published, among them only 1 case in a female patient (Table 1). In all patients (including our patient) ACD was severe. In the male patients the contact dermatitis was localized on the penis, scrotum, buttocks, or thighs, in the female patient on the vulva and inner thighs similar to our case. Additionally, in our patient the vagina was affected.

Our patient developed contact dermatitis 8 days after she had used nifuratel for the 1st time (as it happened presumably in 2 other patients). Thus, it may be assumed that nifuratel is a potent allergen. However, there may be other reasons for this. The inner third of the surface of the labia minora and the vaginal epithelium are more permeable because on the one hand they lack a stratum corneum and are thinner than the epithelium at other sites,

Table 1. Allergic contact dermatitis (ACD) to nifuratel: reported cases

Case no.	Sex/age (years)	Medicament	Localization	Sensitization	Time between application and development of ACD (elicitation)	Reference
1	M, 43	Macmiror® ointment	Genitals	During sexual intercourse, his wife had used Macmiror® vaginal suppositories for about 15 days	5 hr after 1st self-administration	(6)
2	M, 45	Emorril® ointment	Perianal region, buttocks, thighs	Not known, during 1st period of application or during a former use of a nifuratel containing ointment (reported use of different topical agents)	Not reported	(7)
3	M, 38	Macmiror Complex® ointment	Genitals, abdomen, thighs	During sexual intercourse	Not reported, aggravated by sexual intercourse	(8)
4	M, 37	Ointment containing nifuratel	Penis, buttocks	Presumably during 1st period of application	10 days after administration	(9)
5	M, 32	Emorril® ointment	Perianal	Presumably during 1st period of application	2 weeks after 1st administration	(9)
6	F, 53	Macmiror® vaginal suppositories	Vulva, thighs	Not known (probably during the 1st period of application 10 years earlier)	Not reported	(10)
7	F, 40	Inimur® vaginal suppositories	Vagina, vulva, perineum, buttocks, inner thighs	During 1st period of application	8 days after 1st administration	Own case

and on the other hand the larger, more loosely packed cell layers and the lower lipid barrier facilitate penetration (2). Moreover, there are many hair follicles on the labia majora. Penetration further may be facilitated in consequence of damaging the epithelium due to friction and pruritus which often occurs during mycotic infections. Additionally, a topical antimycotic is applied on inflamed skin or mucosa. Sensitization to a hapten needs a danger signal which can be generated by its irritant properties but the inflammatory milieu developing during an infection probably further subserves the sensitization process (3).

In comparison to other topical antimicrobial drugs such as neomycin, framycetin, and clotrimazole, contact dermatitis to nifuratel in genital ACD is rare (4, 5). This may be because of the relatively uncommon use of the substance in comparison to other substances. As a commercial patch test preparation is not available, there may be under reporting of contact allergy to nifuratel.

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