Contact Vulvitis due to Pseudowintera Colorata in a Topical Herbal Medicament

Monica Corazza¹, Maria Michela Lauriola¹, Ferruccio Poli² and Annarosa Virgili¹

¹Department of Clinical and Experimental Medicine, Section of Dermatology, University of Ferrara, Via Savonarola 9, IT-44100 Ferrara, and ²Department of Evolutionistic Experimental Biology, Faculty of Pharmacy, University of Bologna, Bologna, Italy. E-mail: czm@unife.it Accepted June 1, 2006

Sir,

Besides traditional topical and systemic pharmacological treatments for the therapy of vulvovaginal yeast and bacterial infections, numerous over-the-counter medicaments containing natural substances (e.g. tea tree oil, echinacea, sodium caprylate, propolis) are marketed. Patients often prefer alternative medicine and selfprescribe herbal-based products.

We report here an unusual case of acute vulvitis that occurred in a young patient after prolonged topical use of an antifungal herbal preparation.

CASE REPORT

A 16-year-old atopic girl, who presented a persistent vulvar itch, spontaneously used Kolorex[®] cream (Named s.r.l., Italy) and Gyno Canesten[®] cream (clotrimazole 2%) (Bayer, s.p.a., Italy) suspecting a vulvar yeast infection. Both the products had been used in the past.

After 10 days, the symptoms worsened and an acute erythematous oedematous vulvitis developed, making hospitalization necessary (Fig. 1). An allergic contact vulvitis was suspected and the two ointments were suspended. The vulvitis healed with systemic antihistamines, parenteral and topical steroids.



Fig. 1. Allergic contact vulvitis after use of Kolorex® cream.

Table I. Patch test results on Day 2 and Day 3, respectively

	D 1	
	Day 2	Day 3
Standard Italian series		
Nickel sulphate 5%	+	+
Kathon CG 0.01%	+	++
Euxyl K400 1.5%	+	+
Patient's own medicaments		
Gyno Canesten® cream, as is	-	-
Kolorex [®] cream, as is	+++	+++
Constituents of Kolorex [®] cream		
Lactic acid 3% aq	-	-
Aloe barbadensis 10% pet	-	-
Cetyl alcohol 30% pet	-	-
Tocopheryl acetate 10% pet	-	-
Cetheareth 22 30% pet	-	-
Pseudowintera colorata 10% pet	+++	+++
Tea tree oil 5% pet	-	-
Lemon tea tree oil 5% pet	-	_
Potassium sorbate 10% aq	-	_
Cetostearil alcohol 30% pet	-	-

Patch tests with the Italian standard SIDAPA series, Kolorex[®] cream and Gyno Canesten[®] cream were performed (Table I).

Positive reactions to the allergens of the SIDAPA series were not considered relevant for the vulvitis; in fact, they were not present in toiletries and topical products used by the patient. A strong positive reaction to Kolorex[®] cream (+++D2/+++D3) was observed.

We successively carried out patch tests with the components of Kolorex[®] cream, provided by the manufacturer. These tests revealed a positive reaction only to *Pseudowintera colorata* 10% in petrolatum (pet) (+++D2/+++D3) (Table I).

The patient refused further patch tests with the test product at lower concentrations. Patch tests performed with *P. colorata* at concentrations of 0.1%, 1% and 5% pet in 10 controls did not reveal any toxic blistering reaction; only 2 controls showed mild erythema, which disappeared after 4 days.

An allergic contact dermatitis to *P. colorata* was therefore diagnosed.

DISCUSSION

Tea tree oil (*Melaleuca alternifolia*) and KolorXtract[®] (*P. colorata*), both extracts from healing plants of Australia and New Zealand, are widely employed in phytothera-

peutic medicaments for their antimicrobial activity. Both of these substances are constituents of Kolorex[®] cream.

Since some cases of contact allergy to tea tree oil have been recently reported in the literature (1-3), to begin with it was suspected that this component of Kolorex® cream might be responsible for the allergic contact vulvitis in our patient. Unexpectedly, patch tests were positive only to *P. colorata*. The latter, also known as "Horopito" or "Pepper-tree", is a member of the Winteraceae family. The leaves of this plant are a traditional medicine used by the Maori of New Zealand to treat fungal skin infections, venereal diseases, stomach pain and diarrhoea (4).

In 1982 a substance called "polygodial" was obtained from the leaves of *P. colorata* (5). It presents anti-fungal, anti-bacterial (5, 6, 7), anti-inflammatory and even antiallergic properties (8).

In particular, polygodial has been proved to possess a fungicidal activity particularly efficacious against yeasts such as *Candida albicans* and *Saccharomyces cerevisiae* (9); it is also effective against *C. krusei*, *C. utilis*, *Cryptococcus neoformans*, and against filamentous fungi such as *Trichophyton mentagrophytes*, *T. rubrum* and *Penicillium marneffei* (6). Furthermore, Kolorex[®] cream seems to be active even in cases of *Gardnerella vaginalis*.

Polygodial acts as a non-ionic surfactant and inhibits the plasma membrane H⁺-ATPase. It therefore seems to respond to the incessant research for antimicrobial agents with new modes of action capable of overcoming the increase in drug resistance and prevalence of opportunistic infections (9).

The adverse effects of this topical medicament are described only as "negligible and self-limiting" irritant effects (4). However polygodial, the main biologically active constituent of *P. colorata* extract, is a bicyclic sesquiterpene dialdehyde (5, 9); a chemical compound potentially capable of causing contact hypersensitivity

in humans (10). Nevertheless, there are no records of toxicity or reports of sensitization to KolorXtract[®]. Our case appears to be the first reported.

In conclusion, the use of botanical extracts with these purported therapeutic benefits has gained considerable popularity, creating a new dermatological problem: the more these products are used the more their potential for allergic reactions increases. All natural remedies must therefore be regarded as possible allergens and dermatologists' recognition of their adverse effects is increasingly important.

REFERENCES

- 1. Kiken DA, Cohen DE. Contact dermatitis to botanical extracts. Am J Contact Dermatitis 2002; 13: 148–152.
- Crawford GH, Sciacca JR, James WD. Tea tree oil: cutaneous effects of the extracted oil of Melaleuca alternifolia. Dermatitis 2004; 15: 59–66.
- Fritz TM, Burg G, Krasovec M. Allergic contact dermatitis to cosmetics containing Melaleuca alternifolia (tea tree oil). Ann Dermatol Venereol 2001; 128: 123–126.
- 4. Data on File, Forest Herbs Research Ltd, Nelson, New Zealand.
- McCallion RF, Cole ALJ, Walker JRL, Blunt JW, Munro MHG. Antibiotics substances from New Zealand plants II. Polygodial, an anti-Candida agent from Pseudowintera colorata. Planta Med 1982; 44: 134–138.
- Lee SH, Lee JR, Lunde CS, Kubo I. In vitro antifungal susceptibilities of Candida albicans and other fungal pathogens to polygodial, a sesquiterpene dialdehyde. Planta Med 1999; 65: 204–208.
- Kubo I, Taniguchi M. Polygodial, an antifungal potentiator. J Natl Prod 1988; 51: 22–29.
- Cunha FM, Frode TS, Mendes GL, Malheiros A, Cechinel Filho V, et al. Additional evidence for the anti-inflammatory and anti-allergic properties of the sesquiterpene polygodial. Life Sci 2001; 70: 159–169.
- Kubo I, Fujita K, Lee SH. Antifungal mechanism of polygodial. J Agric Food Chem 2001; 49: 1607–1611.
- Warshaw EM, Zug KA. Sesquiterpene lactone allergy. Am J Contact Dermatitis 1996; 7: 1–23.