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Eczematous erythroderma induced by cyanamide

PATRICIA ABAJO, CARLOS FEAL, TATIANA SANZ-SÁNCHEZ, JAVIER SÁNCHEZ-PÉREZ AND AMARO GARCÍA-DÍEZ

Department of Dermatology, Hospital Universitario de la Princesa, C/Diego de León 62, 28006 Madrid, Spain

Key words: cyanamide; anti-alcoholic drugs; adverse drug reactions; erythroderma; systemic contact dermatitis; positive patch test. © Munksgaard, 1999.

The term cyanamide is applied to both free cyanamide (carbimide) and its calcium salt (calcium carbimide). It is extensively used as a fertilizer, herbicide and chemical intermediate (1). In the medical field, cyanamide was introduced into Canada, Europe and Japan in 1956 as a treatment for chronic alcoholism. It acts by interfering with the hepatic metabolism of ethanol by inhibiting aldehyde dehydrogenase. When this transformation does not take place, there is an increase in acetaldehyde in the blood, resulting in unpleasant sensations (2). The rare adverse skin reactions due to cyanamide include allergic contact dermatitis (3–7), lichen planus (8, 9) and lichenoid eruption (9).

Case Report

A 61-year-old man presented to our Department in April 1997 with no family or personal history of atopy, with a past medical history of laryngeal cancer, chronic bronchitis and alcoholic hepatopathy, and receiving treatment with Colme® (calcium cyanamide) since January 1997, and paracetamol and Benerva® (thiamine) for 1 month. He gave a 1-month history of pruritic, erythematous scaly lesions that had started on the upper eyelids and spread in a few days to the face, trunk and

extremities, including the palms and soles. He did not report fever. Physical examination revealed universal redness and scaling of the skin (erythroderma), favouring the antecubital and popliteal fossae, and also the palms and soles. The oral mucous membranes were not involved, neither was there hair loss. He had no lymphadenopathy or hepatosplenomegaly. Laboratory studies showed the following abnormal values: MCV 100 fl (83–97 fl), ALT 63 U/L (1–40 U/L) and GGT 59 U/L (1–50 U/L). Biopsy of a cutaneous lesion showed hyperkeratosis with parakeratosis, irregular acanthosis with spongiosis and some epidermal microvesicle formations, and perivascular infiltrates of round cells in the papillary dermis. The lesions resolved in a week once Colme® was discontinued, and treatment with oral and topic corticosteroids and emollients were started, and did not relapse.

The patient was patch tested with the GEIDC standard series, Benerva® 10% aq. and pet., paracetamol 0.1% pet. and Colme® 10% and 50% aq., with positive reactions to nickel sulfate at D4 and Colme® 10% and 50% aq. at D2 and D4 (Table 1). Subsequently, we patch tested him with the components of Colme®: cyanamide 0.1%, 0.5%, 1% and 5% aq., sorbic acid 2% and 5% pet., and acetic acid 3% aq., with positive reactions only to cyanamide at D2 and D4 (Table 1). 20 controls were tested with cyanamide 5% aq., all of them being negative.

Discussion

Our patient presented with erythroderma, favouring the antecubital and popliteal fossae, with histopathological findings of spongiotic dermatitis, which resolved in a week once Colme® was discontinued. Patch tests with Colme® 10% and 50% aq., and with cyanamide 0.1%, 0.5%, 1% and 5% aq. were positive at D2 and D4. To our knowledge, this is the 1st report of eczematous erythroderma induced by cyanamide (Colme®). With reference to systemic reactions induced by cyanamide, there are only 2 reports that describe 8 patients with lichen planus and lichenoid dermatitis (8, 9). Histopathologic findings were similar in all of them, reflecting a lichenoid dermatitis.

Table 1. Patch test results

Allergens	Concentration and vehicle	D2	D4
GEIDC standard series			
nickel sulfate	2.5% pet.	–	+
Colme®	10% aq.	+	++
Colme®	50% aq.	++	++
cyanamide	0.1% aq.	+	+
cyanamide	0.5% aq.	+	++
cyanamide	1% aq.	++	++
cyanamide	5% aq.	++	++
sorbic acid	2% pet.	–	–
sorbic acid	5% pet.	–	–
acetic acid	3% aq.	–	–

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Value of patch tests in pristinamycin-induced drug eruptions

C. MAYENCE, A. DOMPMARTIN, L. VERNEUIL, M. MICHEL AND D. LEROY

Department of Dermatology, Centre Hospitalier Universitaire, Avenue Georges Clemenceau, 14033 Caen, France

Key words: pristinamycin; antibiotics; synergists; adverse drug reactions; acute generalized exanthematous pustulosis; virginiamycin; cross-sensitivity; positive patch test. © Munksgaard, 1999.

Patch testing is worthwhile in maculopapular (1, 2), eczematous (3) and pustular drug eruption (4, 5), because in approximately 20% of such patients the implicated drug is positive (6). The synergist antibiotic pristinamycin can induce adverse skin reactions (7–9).

Patients and Methods

Between 1989 and 1998, 11 patients (6 female, 5 male, mean age 51 years $\pm$ 16) presented with a cutaneous drug reaction after oral pristinamycin. All patients cleared after discontinuing the drug. 4 patients also had a history of contact dermatitis from virginiamycin. Imputability for pristinamycin was high (10), because it was the only drug recently introduced except in 2 patients. We had 30 patients in a control group (13 female, 17 male, mean age 67 years $\pm$ 15), who had all been treated with pristinamycin within the last 3 months without adverse reaction.

Patch tests were performed 1 to 3 months after treatment with pristinamycin. A tablet of pristinamycin (Pyostacine[®], Specia, Paris, France) was crushed and di-

luted 20% aq. and 20% pet. Other suspected drugs were also tested in 2 patients. Patch tests were performed with Finn Chambers on Scanpor (Epitest, Tuusula, Finland) and applied on the upper back. The tests were read 2 days later according to ICDRG guidelines.

Results

Of the 11 patients, 9 had a positive patch test to pristinamycin in aq. and pet. The pristinamycin test was the only one positive in the 2 patients who had taken other drugs. There was no relapse of the drug eruption during patch testing. Patch tests were negative in the 30 control patients (Table 1).

Discussion

The most frequent adverse effects of pristinamycin are cutaneous reactions (11). The 1st cases were reported in 1986 by Tomb & Grosshans (12) after local sensitization with virginiamycin. Bleumink & Nater (13), Lachapelle & Lamy (14), and Baes (15) had previously emphasized cross-reaction between virginiamycin and pristinamycin. We ascertained that 4 patients had previously used a topical preparation containing virginiamycin. Pristinamycin contains a well-known sensitizer, fraction IIA, which represents 45 to 60% of the molecular weight (16). The eruption may be a combination of an immediate-type and a delayed-type immune reaction. Eczematous lesions, and previous contact with virginiamycin, are in favour of systemic dermatitis (17).

It remains difficult to make an accurate diagnosis of drug-induced eruptions. In vitro tests are rarely reliable (18). Positive patch test results were obtained in 30% of patients presenting with a maculopapular drug rash (2).

Table 1. Patch test results

Cutaneous manifestations in patients treated with pristinamycin	No. patients tested	No. patients with positive pristinamycin patch tests
maculopapular rash	5	3
eczematous eruption	3	3
acute generalized exanthematous pustulosis	3	3
no eruption (controls)	30	0