

Contact dermatitis from dicyclohexylcarbodiimide

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Introduction

Dicyclohexylcarbodiimide (DCCI) is a coupling agent used in peptide synthesis, to which chemists may become exposed and sensitized. Our report of 4 cases from the same manufacturing process and employer adds to the limited literature on this compound, which is both a sensitizer and an irritant, and reflects on previous knowledge.

Case 1

A 28-year-old female research chemist, working with valaciclovir, presented with face and neck dermatitis. Initial patch tests with valaciclovir and dicyclohexylurea were negative. Her medical history included allergic rhinitis, but not atopic dermatitis though she did have a sister with atopic dermatitis.

On returning to the valaciclovir process in her laboratory, the patient noted recurrence of the rash within 2 days, in the form of facial dermatitis with secondary spread to her upper and lower limbs. Some areas were vesicular. Significantly, isolated areas on her left forearm, right cheek, and right ear had been exposed to a splash of laboratory chemicals, resulting in a localized dermatitis that appeared on the night of the exposure.

Therefore, patch tests were repeated with the standard series plus chemicals implicated in the splash: DCCI 0.1% petrolatum (pet.); dimethylformamide 0.1% pet.; acyclovir 5% pet.; z-valine 0.1% pet.; and dimethylaminopyridine 0.1% pet. The suitability of 0.1% pet. (w/w) as a patch test preparation for DCCI has previously been determined (1).

DCCI was ++ on day (D)2 and + on D4, which was clearly of current relevance. A + reaction to nickel sulfate 5% pet., of past relevance, was also noted.

Case 2

6 months later, a 29-year-old female research chemist from the same employer also working on the

valaciclovir process presented with neck dermatitis. Her past history included atopic dermatitis. She was removed from the process and the rash resolved. When she was reinstated, the rash returned. She was similarly patch tested, resulting in a +++ reaction to DCCI 0.1% pet. on D2 and D4.

Case 3

A further case, a 28-year-old male analytical chemist with known atopic dermatitis, presented with flexural, neck and wrist dermatitis. His atopic dermatitis had settled in his teenage years, although there was some seasonal deterioration in his skin in winter. While working on the valaciclovir process, the dermatitis flared with fissuring, particularly, within 3 days returning to the laboratory from days off. As with the above cases, his dermatitis improved significantly after being removed from the laboratory. Patch testing to DCCI 0.1% pet. showed a +/- reaction on D2 and + on D4. A repeat test showed a + reaction on D2. Other patch tests including the standard series, medicaments, and other chemicals from the laboratory process were negative.

Case 4

Finally, a process chemist, also working on the valaciclovir process, presented with flexor and extensor wrist dermatitis. The 35-year-old man, with no history of atopy or past skin disease developed symptoms while working in the laboratory, but has been in complete remission for 1 year since leaving the process. Patch testing to DCCI 0.1% pet. elicited a ++ reaction on both D2 and D4, while other chemicals in the process and the standard series were negative, as in the above cases.

Discussion

Allergic contact dermatitis has previously been reported from DCCI, and initially a patch test

concentration of 0.1% in acetone was noted to be useful in humans, as higher concentrations caused irritation (2). Following the report that a 0.1% concentration in pet. was also suitable for elicitation in patch tests (1), other investigators have also used this preparation (3, 4).

As DCCI is used in peptide synthesis, the original report (2) suggested that the incidence of DCCI sensitization might increase as this laboratory technique became more widespread. Hoffman and Adams (4) describe a DCCI-sensitized research chemist who was able to return to work without recurrence of symptoms if protective clothing and a ventilated hood were used. Nevertheless, 2 reports involve research chemists who had been taking precautions and wearing rubber gloves, but who were sensitized despite this, perhaps from minimal exposure (3, 5). Concentrations as low as 0.006% in acetone have sensitized mice, and DCCI is thus considered a potent allergen (6). In this series of four cases, we believe the cause of sensitization was direct skin exposure in subjects who were not adequately using personal protection equipment.

Kato et al. (7) have shown that mice expressing major histocompatibility complex haplotype H-2^k may be specifically unresponsive to DCCI sensitization, but in humans, it remains unclear whether

the low incidence is due to under-reporting, protective measures or even genetic factors.

References

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