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Cutaneous adverse drug reaction induced by oral dexamethasone with possible cross-reactivity to Group 1 corticosteroids confirmed by patch testing and intradermal testing

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Whilst a recent large study from Europe reported that 1.2% of patch-tested patients have corticosteroid contact hypersensitivity¹, cutaneous adverse drug reactions (CADR) due to systemic corticosteroids are less well described². Coopman and colleagues originally defined four classes of corticosteroids according to their structure (A/B/C/D)³, however a recent simplified classification system proposed by Baeck and Goossens has refined this further into three different groups (1/2/3)⁴. Cross-reactivity does not always follow this categorisation. Here we report a novel case of a CADR induced by oral dexamethasone with possible cross-reactivity to Group 1 corticosteroids.

CASE REPORT

An 80-year-old male underwent dental implant surgery and was subsequently started on oral dexamethasone, clindamycin and metronidazole. Forty-eight hours later he developed a generalized maculopapular exanthema, which resolved over the course of seven days following medication discontinuation. He reported no previous reactions to corticosteroids.

Intradermal testing was later performed with the diluted (0.9% NaCl) stock concentrations of dexamethasone (1:10 of 3.3mg/ml), clindamycin (1:10 of 150mg/ml), and metronidazole (1:10 of 5mg/ml). On delayed reading at 48-hours there was a strong positive reaction to dexamethasone only, with an exuberant

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bullous lesion at the testing site (Figure 1). We then conducted cross-reactivity studies via patch testing using IQ Ultra chambers with a corticosteroid series (Chemotechniques Diagnostics, Vellinge, Sweden). The patch tests were read on day (D) 2 and D4 in accordance with ICDRG criteria, following 48-hours of occlusion. Patch testing revealed strong positive (++) reactions at D4 to tixocortol pivalate (0.1% petrolatum (pet)) and dexamethasone disodium phosphate (1% pet), with negative responses to the remainder of the corticosteroid series tested (budesonide (0.01% pet), clobetasol propionate (1% pet), betamethasone valerate (1% pet) and hydrocortisone butyrate (1% alcohol) (Figure 2). Further intradermal studies were also conducted with triamcinolone acetonide (1:10 of 40mg/ml), hydrocortisone sodium succinate (1:10 of 50mg/ml), and methylprednisolone (1:10 of 40mg/ml); which revealed positive reactions at 48-hours to hydrocortisone and methylprednisolone only (Figure 2).

He was diagnosed with oral dexamethasone induced CADR, with additional evidence of possible cross-reactivity to Group 1 corticosteroids. We later also conducted an intramuscular provocation test with triamcinolone acetonide (40mg) and a topical challenge test with clobetasol propionate ointment; both of which were tolerated without any adverse delayed reaction and were thus recommended as safe alternatives for future use

DISCUSSION

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Here we report, to the best of our knowledge the first case of a CADR induced by oral dexamethasone with evidence of possible Group 1 corticosteroid cross-reactivity confirmed on patch testing and intradermal testing. Systemic (delayed-type) hypersensitivity to corticosteroids has been observed in cases of previous contact sensitization to topical corticosteroids, whereby a systemic contact dermatitis develops when corticosteroids are administered via oral or parenteral routes⁵. However, prior contact sensitisation is not a mandatory requirement for all CADR to corticosteroids^{2,5}. Dexamethasone has been reported to induce generalized exanthemas, as have other corticosteroids (i.e. betamethasone) following systemic exposure². Whilst the current simplified classification system (Baeck and Goossens) groups the corticosteroids according to molecular structure (Group 1, 2 or 3), this was predominantly designed for contact allergy⁴. Cross-reactivity within these groups has certainly been described⁶, however growing evidence suggests that cross-reactivity also occurs amongst corticosteroids belonging to different groups^{6,7}. The current simplified classification system is therefore unable to explain all observed cross-reactions and is thus not always accurately predictive⁸. Furthermore, less is known about classification and cross-reactivity of less common delayed-type hypersensitivity reactions to corticosteroids following systemic administration⁴. In our report the patient reacted to dexamethasone (Group 3) and likely cross-reacted to select Group 1 corticosteroids (i.e. hydrocortisone, methylprednisolone), without reacting to Group 2 (i.e. budesonide) or other corticosteroids from Group 3 (i.e. clobetasol propionate). This rare occurrence has not been previously reported with

systemic dexamethasone, although cross-reactivity between desoximetasone (Group 3) and Group 1 corticosteroids has been described in the contact allergy literature⁹. Corticosteroid cross-reactivity is therefore more complex than just structural homology and likely also involves drug metabolism and stereoisomerism¹⁰.

In conclusion, we describe a novel case of a CADR due to oral dexamethasone with possible cross-reactivity to Group 1 corticosteroids. We highlight the utility of patch testing, intradermal testing and provocation tests in safely identifying the culprit agent, potential cross-reactive drugs and safe alternatives. Future studies into the cross-reactivity of corticosteroids in CADR would be beneficial.

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Figure Legends

Figure 1. Intradermal test results at 48-hour reading for **(A)** Dexamethasone (positive with bullous lesion), **(B)** Clindamycin (negative) and **(C)** Metronidazole (negative).

Figure 2. Additional intradermal test [Left Panel] and patch test [Right Panel] results for **(A)** Hydrocortisone sodium succinate (positive), **(B)** Methylprednisolone

(positive), **(C)** Triamcinolone acetonide (negative), **(D)** Tixocortol pivalate (++), **(E)** Budesonide (negative), **(F)** Clobetasol propionate (negative), **(G)** Betamethasone valerate (negative), **(H)** Dexamethasone disodium phosphate (++) and **(I)** Hydrocortisone butyrate (negative). Intradermal result photo was taken at 48-hours and patch test result photo was taken at Day 4 reading.

Figure 1

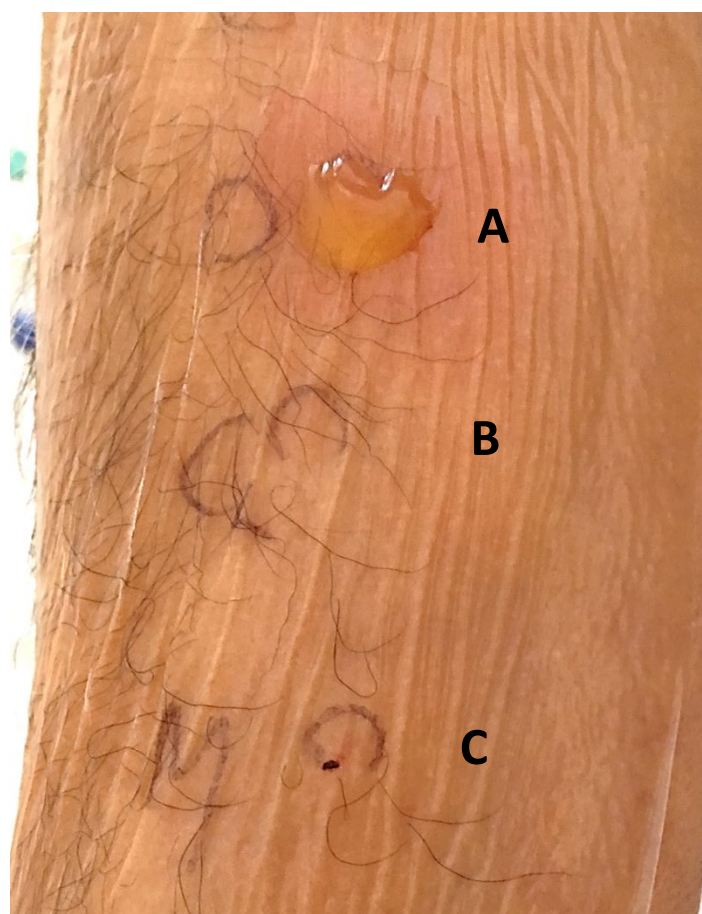


Figure 2

