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Systemic contact dermatitis following oral exposure to tramadol in a patient with allergic contact dermatitis caused by buprenorphine

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Allergic contact dermatitis is typically observed when the skin of a sensitized person is re-exposed to the causative allergen. However, in rare cases, a cutaneous allergic reaction may develop after systemic exposure to a hapten (1). Buprenorphine, a strong opioid analgesic, is a semisynthetic derivative of the morphine alkaloid thebaine, which partially binds to the μ -opioid receptor and has an agonist function (2). It is available for parenteral, sublingual and transdermal administration for the treatment of chronic and moderate-to-severe pain (3). Severe skin reactions caused by buprenorphine are rarely observed, and only a few cases of allergic contact dermatitis have so far been reported (4, 5). Systemic allergic contact dermatitis following oral exposure to tramadol has, to our knowledge, not previously been described. We diagnosed and treated a patient with strong patch test reactivity to Norspan[®] patches containing buprenorphine and who developed systemic allergic contact dermatitis following oral exposure to tramadol.

Case History

A 52-year-old non-atopic woman, suffering from joint pain resulting from Ehlers–Danlos syndrome, was referred to our department with allergic contact dermatitis on her shoulder after prolonged cutaneous exposure to Norspan[®] patches containing buprenorphine, at a concentration of 10 mg/hr, to be changed every seventh day. Patch testing was performed with the European

baseline series and an extended patch test series including buprenorphine 0.3 mg/ml in pet. We used Finn Chambers[®] (8 mm; Epitest Ltd, Oy, Finland) on Scanpor[®] tape (Norgesplaster A/S, Alpharma, Venne, Norway). Patches were applied to the upper back and were occluded for 48 hr. Readings were performed on day 2 and day 5 according to the recommendations of the International Contact Dermatitis Research Group (6). A positive reaction (+) to buprenorphine was identified on day 2 and on day 5. Additionally, an allergic reaction to (++) to palladium chloride 2% pet. was identified.

At the Multidisciplinary Pain Centre in Copenhagen, the patient was prescribed oral treatment with tramadol retard (200 mg twice daily). Within 24 hr of treatment, a severe systemic allergic dermatitis reaction was observed at the site of the Norspan[®] patch, with homogeneous infiltration, vesicles, and bullae, as well as an orange–red discoloration, and systemic symptoms, including influenza-like symptoms, fever, and shivering. No baboon syndrome was observed.

To test whether the patient was contact allergic to other opioids (synthetic and non-synthetic morphine derivatives), patch testing, prick testing, intradermal testing and oral provocation testing were performed with morphine, methadone and ketogan, and all were all negative. Hence, Duragesic[®] patches containing fentanyl were recommended as analgesic treatment, and at the time of publication no allergic contact dermatitis has been observed.

Discussion

Systemic allergic contact dermatitis after oral exposure to tramadol has not previously been described in the literature. However, cutaneous side-effects of opioid analgesics are well known, including urticaria, flushing, and pruritus, which are typically caused by non-immunological

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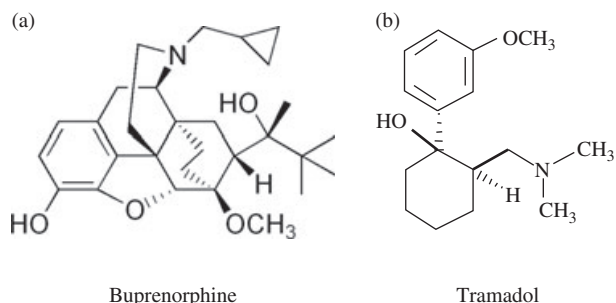


Fig. 1. (a) Buprenorphine; chemical structure. (b) Tramadol; chemical structure.

histamine release triggered by opioids. Also, delayed-type hypersensitivity reactions have been reported,

with codeine being the most frequent allergen (7). Furthermore, patch test cross-reactivity between codeine, morphine and heroin has been observed (7, 8), whereas no cross-reactivity has been reported between chemically unrelated opioids such as fentanyl or tramadol (7, 8). The observed concomitant reactions to Norspan[®] patches and tramadol may be attributable to their similar chemical structures, as they belong to the same chemical group of opioids (Fig. 1).

It is important for clinicians to be aware of the risk of development of systemic allergic contact dermatitis, especially in patients with previous allergic contact dermatitis. In our patient, fentanyl would have been a useful alternative, and this could also be the case in other patients who develop skin sensitivity, as it seems to be better tolerated.

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