

CONTACT POINTS

Cimetidine and racecadotril: Unusual culprit drugs of a severe cutaneous adverse reaction

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Allergy to cimetidine or racecadotril is rarely encountered in clinical practice. Patch tests (PT) and oral provocation tests (OPT) are both useful to detect the culprit drug(s) in cutaneous adverse drug reac-

tions (CADR). Herein, we report the case of a severe CADR with sensitization to cimetidine and racecadotril, confirmed by OPT and PT, respectively.

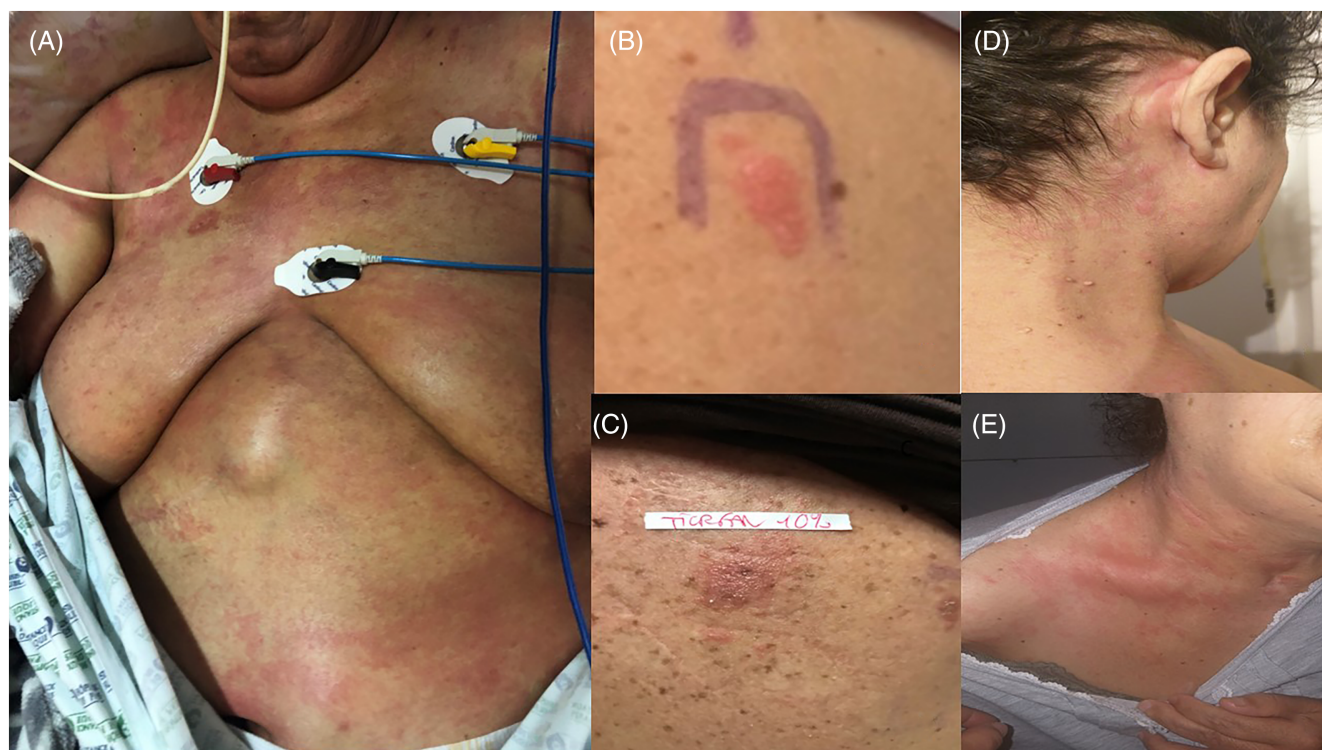


FIGURE 1 (A) Patient with diffuse maculo-papular exanthema; (B) positive (++) patch test on day 2 (D2) to racecadotril 17% pet.; (C) positive (+++) patch test on D2 to racecadotril 10% pet; (D and E) maculopapular exanthema on day one of full dose of cimetidine reintroduction

CASE REPORT

A 62-year-old patient was referred for an allergy work-up 10 months following a 'probable' DRESS (Regiscar score 4) associated with fever, diffuse exanthema, facial edema, high eosinophil blood count (2900/ μ l) and EBV replication as shown by PCR.¹ The patient was successfully treated with ultrapotent topical corticosteroids. The CADR occurred during a hospitalization for the exploration and management of biliary hepatic duct dilation secondary to a hydatid cyst. Possible culprits were cimetidine (started 11 days [D] before the skin rash, to prevent gastric ulcers), racecadotril (started 8D before the rash, for a non-infectious diarrhoea), acetazolamide (started 7D before the rash) and enoxaparin (started 37D before the rash) (Figure S1). Allergy testing was performed following international recommendations with PT (readings at D2 and D4) and late readings (D3) of prick and intradermal tests (IDT).^{2,3} PT with pure enoxaparin, acetazolamide 10% pet. and cimetidin pills 30% pet. (final concentration of active ingredient [AI] = 2.5%) were negative. Racecadotril PT (pills 30% pet.; AI 17%) were positive (++/++), confirmed by a new PT with AI 10% (+++) (Figure 1). IDT with enoxaparin and acetazolamide, and a prick test with cimetidine (not available in par-enteral form) were also negative. Progressive challenge (1/10th, followed a week later by the full dose) of enoxaparin, and then acetazolamide, were negative. Upon OPT of 1/10th of the cimetidine dose, the patient complained of pruritus on D2, without exanthema, but a diffuse maculo-papular exanthema developed on D1 after administration of the full dose (Figure 1). Hypersensitivity for cimetidine and racecadotril was thus demonstrated.

DISCUSSION

To the best of our knowledge, we report the first case of drug hypersensitivity to racecadotril confirmed by a positive PT. Only one case of 'non-allergic hypersensitivity reaction' has been described, in a child, with a negative PT at 10%.³ Cimetidine is widely prescribed, with a favourable safety profile⁴; few cases of severe CADR have been previously attributed to it, but no cases of DRESS, and without any positive PT.⁵⁻⁷

Skin tests are the cornerstone to identify culprits in drug allergies. In case of negative tests, the gold standard to identify causal drugs is the OPT. In our case, we did not perform OPT for racecadotril because of the positive PT, knowing that we already had six negative PT controls (personal unpublished data), in addition to the negative control reported by Nucera et al.,³ emphasizing the good value of our positive PT. Furthermore, there is a risk of relapse in DRESS when challenging drugs that tested positively on patch.^{2,8} The positive cimetidine OPT, 10 months after the initial DRESS, points towards polysensitization, in spite of the negative PT. Multiple drug hypersensitivity may occur during DRESS, and relates to a long-lasting, massive T-cell stimulation, even to drugs with chemically unrelated structures, as occurred in our patient.⁹ This constitutes a major issue in the

management of such patients, especially when it concerns multiple, and sometimes potentially life-saving drugs.^{8,10} To conclude, in DRESS, all potential culprits must be tested, even those rarely reported in the literature, and a careful OPT can sometimes be performed.^{2,5,10,11}

CONFLICT OF INTEREST

The authors have no conflict of interest to disclose.

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SUPPORTING INFORMATION

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