

Erythema multiforme-like eruption induced by risedronate

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doi:10.1111/cod.12839

Key words: bisphosphonates; case report; cutaneous adverse drug reactions; erythema multiforme-like eruption; non-immediate reactions; patch test; risedronate.



Fig. 1. Erythema multiforme-like eruption involving the left upper limb and left hand; (a) positive patch test reaction to risedronate (++ on day 4).

Risedronate sodium [CAS no. 115436-72-1, *P,P'*-(1-hydroxy-2-(3-pyridinyl)ethylidene) bis-phosphonic acid sodium] is a bisphosphonate that is used to prevent and treat osteoporosis. Cutaneous adverse drug reactions (CADRs) induced by risedronate are rare (1); among these, erythema multiforme-like eruption has never been reported.

Case Report

A 56-year-old non-atopic woman presented with an itchy erythema multiforme-like eruption mainly involving the upper limbs and hands (Fig. 1). The reaction had appeared a few days after the first course of oral therapy with risedronate (75 mg daily for 2 consecutive days every month)

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Conflicts of interest: All authors have no interests to report.

for postmenopausal osteoporosis. A full laboratory panel of investigations, including autoimmunity and coagulation tests, inflammatory markers, and a broad viral panel, gave negative results. The eruption disappeared within 2 weeks with the application of topical desoxymethasone (twice daily) and oral oxatomide (30 mg twice daily). Risedronate therapy was stopped, and 3 months later patch tests with the Società Italiana di Dermatologia Allergologica Professionale e Ambientale (SIDAPA) baseline series (FIRMADAGENT[®], Florence, Italy) and three bisphosphonates (risedronate 7.5%, alendronate 7%, and ibandronate 7.5%, all in pet.) were performed. Allergens were occluded for 48 h with Haye's Test Chambers[®] (Haye's Service, Alphen aan den Rijn, The Netherlands) on Soffix[®] tape (Artsana, Grandate, Italy), and read on day (D) 2 and D4 to D7 according to ESCD guidelines (2). Patch tests showed positive reactions to risedronate 7.5% pet. (++) at D2 and D4 (Fig. 1a). Twenty healthy volunteers were patch tested with the same risedronate preparation, with negative results. On the basis of this, our patient again started osteoporotic therapy with alendronate, without any recurrence during the subsequent 2 years of follow-up.

Table 1. Reported cutaneous adverse drug reactions to risedronate

Study	Clinical picture	No. of cases
Barrera et al. (1)	Rash	29
	Pruritus	4
	Urticaria	3
	Photosensitivity	2
	Hair loss	1
	Skin irritation	1
	Stevens–Johnson syndrome	1
	Xerosis	1
Anastasilakis et al. (3)	Rash and pruritus	1
Belhadjali et al. (4)	Cutaneous vasculitis	1
Vidal (5)	Rash	3–4% of treated cases
	Pruritus	2% of treated cases
FDA (6)	Stevens–Johnson syndrome	5
	Toxic epidermal necrolysis	2

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Discussion

Bisphosphonates are widely used to treat postmenopausal and corticosteroid-related osteoporosis and to prevent the risk of osteoporotic fractures. They are divided in two classes that work differently in killing osteoclast cells: the non-N-containing class (clodronate, etidronate, and tiludronate) and the N-containing class (alendronate, ibandronate, neridronate, olpadronate, pamidronate, risedronate, and zoledronate). Among these, risedronate is considered to be safe and well tolerated (1), and CADR are relatively rare (1, 3–6), hitherto not including erythema multiforme-like eruption confirmed by a positive patch test reaction (Table 1). Negative patch test results with other two bisphosphonates belonging to the same N-containing class (alendronate and ibandronate) showed no cross-reactivity to these compounds.

This report confirms the value of patch testing in non-immediate CADR, such as erythema multiforme-like eruption (7). Furthermore, patch tests showed the absence of cross-reactions among the tested bisphosphonates, allowing us to treat our patient's osteoporosis with alendronate with good tolerance.