

Desensitization of epoetin- α in a confirmed case of acute exanthematic pustulosis

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Human recombinant erythropoietins are widely used for anemias associated with chronic kidney disease (1). Allergic reactions to erythropoietin have only occasionally been reported.

Skin reactions include pruritus, wheals at the injection site, orofacial angioedema and anaphylaxis, suggestive of immediate type allergic hypersensitivity (2).

We report the case of a man who experienced three episodes of acute generalized exanthematous pustulosis after human recombinant erythropoietin. A desensitization protocol with epoetin- α was successfully carried out and the patient has tolerated the drug in subsequent therapeutic courses.

An 88-year-old man with renal failure due to chronic high blood pressure (hypertension) and no history of allergy initiated therapy with epoetin- α (6000 IU/week subcutaneously). At the second administration, 2 weeks after the first, the patient developed pruritus with erythema on the forearms, which resolved with antihistamines and drug discontinuation.

After resolution, at a subsequent administration an erythematous maculopapular eruption appeared on the forearms plus legs and gluteal area, more intense than the previous episode and requiring corticosteroids and antihistamines. The symptoms subsided completely in 10 days.

Two weeks later, epoetin- α was replaced by darbopoetin- α (40 μ g) but the patient again experienced a similar episode in both symptoms and location. Skin biopsy revealed parakeratosis, intraepidermal pustules filled with neutrophilic leukocytes, and a perifollicular lymphocytic infiltrate in the dermis with the presence of a slight eosinophilia. A diagnosis of acute exanthematic pustulosis was made.

Epicutaneous (10 000 IU) and intradermal testing with different concentrations of epoetin- α (100, 1000 and 10 000 IU) and darbopoetin- α (0.4, 4 and 40 μ g) gave no positive reactions at 20 min or 24, 48 and 72 h after application.

A two-day controlled administration of epoetin- α was designed to achieve a total therapeutic dose of 2000 IU (16.8 μ g) (Table 1). The night before and 30 min before the initiation of the protocol the patient was premedicated with cetirizine 10 mg, ranitidine 150 mg and prednisone 60 mg. The patient tolerated the full therapeutic dose with no adverse effects and continues with a

maintenance dose of 3000 IU administered twice weekly. He was discharged from the Allergy Service and this treatment is now supervised by the Nephrology Service.

Acute generalized exanthematous pustulosis is a severe eruption which is usually drug related, although viral agents have also been involved (3). The diagnosis was based on two reproducible episodes and the histopathological characteristics. Because of the need to give this drug in this case, a desensitization approach was considered and achieved successfully.

Several questions concerning the mechanism of long-lasting tolerance are raised. Although initial tolerance can be attributed to the premedication, this seems unlikely because the initial dose was not continued. The reason for the use of corticosteroids and antihistamines was to prevent a potential adverse effect during the course of desensitization. Another explanation for the tolerance was that the patient was in a refractory status due to the short interval since the previous allergic episode, as has been reported for cases with fixed drug eruption (4). Whether this phenomenon occurs in acute generalized exanthematous pustulosis is not known but it remains possible.

To our knowledge, this is the first report of acute generalized exanthematous pustulosis due to a human recombinant erythropoietin. As the patient needed treatment with this drug we undertook a rational approach aimed at achieving tolerance. Because of the severity of the reaction we considered it appropriate to use a pretreatment just at the start. Whether the good tolerance was due to a true desensitization or to a refractory period is unknown.

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A desensitisation approach in a subjects with a proven acute exanthematic pustulosis induced by epoetin-a was successfully achieved. After completion, the subject continued the treatment with good tolerance.

Table 1. Epoetin- α desensitization regimen

	Dose (IU)	Time interval	Cumulative dose (IU)
Day 1	100	1 h	100
	200	1 h	300
	400	1 h	700
	400	1 h	1100
Day 2	1000	1 h	1000
	1000	1 h	2000

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