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Desensitization of Darbepoetin-α: A Case Report

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Summary
Human recombinant erythropoietins (EPO) and darbepoetins are widely used for anemias associated with chronic kidney disease. Allergic reactions to erythropoetins and darbepoetins have only occasionally been reported. These skin reactions include pruritus, wheals at the injection site, orofacial anaphylaxis and anjioedema. In this article, we report an 11 year-old female who experienced generalized erithematous skin eruption and desquamation after both erythropoietin and darbepoetin treatments. We successfully used darbepoetin with the support of premedication and desensitization.

Introduction

Recombinant human erythropoietin (EPO) was first used for the treatment of renal anemia in 1986. Since then, millions of patients have treated EPO for correction of renal and **non-renal** anemias. Recombinant EPO preparations are produced by different manufacturers (epoetin-α and epoetin-β). Allergic reactions to erythropoietin include pruritus, wheals, anaphylaxis and angioedema, suggestive of immediate type allergic hypersensivity. Darbepoetin-α is a glycoprotein analogue of recombinant human erythropoietin. The number of the cases published on allergic reaction to dabepoetin is limited in the literatüre (1-4). In this article, we report an 11 year-old female with renal failure due to vesicoureteral reflux (VUR). She experienced erythematous maculo-papuler eruption and intensive skin desquamation after recombinant human erythropoietin (EPO) and darboepoetin treatment. A desensitization protocol with darbepoetin-α was successfully performed and the patient has tolerated the drug in subsequent therapeutic doses.

Case

An 11 year-old young girl had renal failure due to bilateral vesicoureteral reflux (VUR). She had no history of atopy and drug allergy. At first, she tolerated therapy with epoetin-α (150 IU/kg/week, subcutaneously) well. At the second administration, the patient developed allergic reactions after two days. Allergic reactions included pruritus, erythematous maculopapuler eruption which disappeared after treatment with antihistamines and drug discontinuation. One month later, erythropoietin was replaced by darbepo-

etin-α (0.75 mcg/kg/week, subcutaneously). But the patient experienced intensive skin reaction (erythematous and desquamation) again at the second day after the drug administration. The symptoms were treated with corticosteroids and antihistamines and subsided completely a week. Skin prick and intradermal testing with different concentrations of darbepoetin-α (1/100, 1/10 and 1/1) gave no positive results at **20 minute and 24 hour, 48 hour, 72 hour** after testing. A two-day controlled subcutaneously application **of darbepoetin-α** desensitization was planned to achieve a total therapeutic dose of 16,250 μg (table). The patient was premedicated with methylprednisolone, diphenhydramine, and ranitidine 13, 7 and 1 hour before desensitization procedure, respectively. The patient tolerated the full therapeutic dose with no adverse effects. The maintenance dose (10μg/week) is now supervised weekly by **nephrology department**.

Discussion

Skin reactions to EPO include pruritus, wheals at the injection site, anaphylaxis, generalized eczema and orafacial anjioedema. Papulomatous skin reactions to EPO have been reported in several patients following several months of treatment and most of them after lasting several weeks cleared up spontaneously (5). Allergic reactions associated with **erythropoietin and darbepoetin** can result from polysorbate 80 excipient. Two cases were reported about polysorbate 80 excipient hypersensivity reactions in the literature. Change to polysorbate-free darbepoetin (Aranesp) did not elicit any reaction (6). A man who has chronic lymphocytic leukemia (CLL) was reported in the literature, after the third darbepoetin injection. The patient developed generalized erythema, swelling, swallowing difficulty, orafacial anjioedema, more severe on the face, neck and arms (3). In another report, generalized urticaria, pruritus, orofacial edema developed after the third dose of darbepoetin. The skin reactions improved after **one** week (7). Desensitization can be considered without any alternative drugs for treatment. Desensitization is a procedure which alters the immune response to the drug and results in temporary tolerance. In the literature, a case that experienced three episodes of acute generalized exanthematous pustulosis after EPO, a desensitization protocol with epoetin-α was successfully performed and the patient tolerated well epoetin-α in following course of treatment (8). Another desensitization report in the literature was from France. The case was an acute generalized exanthematous pustulosis after EPO and epoetin-α desensitization protocol was successfully carried out (9).

In conclusion, to our knowledge, this is the first report about darbepoetin-α desensitization. We successfully used darbepoetin-α with the support of premedication and desensitization. Because of the erythropoietin or darbepoetin treatment was so crucial in these patients; our approach might be a suitable option for them.

Table 1 *- Darboepoetin-α desensitization protocol*

DAY 1		
Dose	Time /Interval	Cumulative dose
250 ng	1 hour	250 ng
500 ng	1 hour	750 ng
1 mcg	1 hour	1,75 mcg
2 mcg	1 hour	3,75 mcg
2.5 mcg	1 hour	6,25 mcg
DAY 2		
5 mcg	1 hour	11,25 mcg
5 mcg	1 hour	16,25 mcg

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