

Clinical case

Two cases of allergy to leucovorin Deux cas de réaction à l'acide folinique

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Received 24 April 2002; accepted 12 March 2003

Abstract

We report two cases of an immediate allergic reaction to leucovorin (folinic acid) with positive skin tests. One patient underwent oral desensitization and was then able to continue complete treatment for a metastatic colon cancer.

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Résumé

Nous rapportons deux cas de réactions immédiates à l'acide folinique avec des tests cutanés positifs évoquant une allergie. Dans un cas, une accoutumance par voie orale a été entreprise afin de poursuivre un traitement complet pour un carcinome colique métastaté.

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Keywords: Leucovorin; Folinic acid; Allergy; Desensitization

Mots clés : Allergie ; Accoutumance ; Acide folinique

Anaphylactic reaction to leucovorin (LCV), a metabolite of folic acid, was reported recently [1]. We report two more cases.

Case 1: A 57-year-old man was treated in 1995 for a rectal cancer with hepatic metastasis. Palliative therapy with fluorouracil and LCV was started. During the first treatment, patient developed diffuse urticaria and breath difficulty shortly after starting the intra-venous LCV. Three months later, skin tests were positive with LCV and negative with folic acid (see Table 1, case 1). The patient was then treated with fluorouracil alone, without further reactions.

Case 2: A 59-year-old man had a colectomy for colon cancer in December 2000, followed by chemotherapy with LCV, fluorouracil and oxaliplatin because of pulmonary and hepatic metastasis. During the initial LCV infusion, the patient developed diffuse urticaria; a similar reaction occurred during the second infusion. Three weeks later, skin tests were

positive with LCV (see Table 1, case 2). Oral desensitization was proposed. Over the following days the patient was given gradually increasing doses of LCV orally to a dose of 375 mg. No reaction occurred, and chemotherapy including LCV was then administered without an adverse reaction.

Five controls from the medical staff had negative skin tests results to the highest tested concentrations of folinic acid positive.

The allergy to LCV was suspected only by skin testing in the present cases. Still, the clinical presentation, the positive skin tests and, in one case, the effectiveness of the desensitization, hypothesized an IgE-mediated reaction. An anaphylactoid reaction caused by non-specific liberation of mediators, like histamine, cannot be excluded, especially because in the both cases the reactions occurred at the first introduction of LCV.

Allergy to LCV was rarely reported. A case of an 80-year old woman who experienced anaphylactic shock during perfusion of LCV, used as in our cases for colic cancer, has been recently reported [1]. In that case and in ours, specific serum IgE was not sought. A limited number of case reports de-

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Table 1
Results of skin tests

Skin prick tests	Flare-Erythema (mm)					
(a) Case 1						
Negative test, serum	0–0					
Positive test, codeine phosphate 9%	10–40					
Calcium folinate, 200 mg/ml	6–40					
Lederfoline [®] , calcium folinate, 50 mg/ml	9–45					
Spéciafoldine [®] , folic acid, 5 mg/ml	0–0					
Intra-dermal tests						
Intra-dermal negative control, serum	0–0					
Dilution	1:1000	1:100	1:10	Pure		
Folinic acid, 200 mg/ml	5–45	–	–	–		
Lederfoline [®] , calcium folinate, 50 mg/ml	0–0	6–45	–	–		
(b) Case 2						
Negative test, serum	0–0					
Positive test, histamine	8–30					
Calcium folinate, 0.2 mg/ml (dilution 1:1000)	0–0					
Calcium folinate, 2 mg/ml (dilution 1:100)	0–0					
Calcium folinate, 20 mg/ml (dilution 1:10)	0–0					
Intra-dermal tests						
Intra-dermal negative control, serum	0–0					
Dilution	1:100 000	1:10 000	1:1000	1:100	1:10	Pure
Calcium folinate, 200 mg/ml	0–0	0–0	0–0	10–20	–	–

scribe immediate hypersensitivity reactions to oral and parenteral folic acid [2,3]. LCV is the active metabolite of the folic acid. Folic acid is constituted by a pteridin group associated with *para*-amino benzoic acid and glutamic acid. The activation of folic acid is obtained by two enzymatic reductions with appearance of tetra hydrofolic acid (or folinic acid or LCV). The existence of folic acid specific IgE was demonstrated in one patient with cross-allergenicity between folic acid and LCV [3]. Binding of folic acid to proteins seems to be necessary to induce an immunologic reaction. The extended use of LCV for the treatment of rectal and colic cancer expose to higher incidence of allergic reactions [4,5]. Desensitization is an effective therapeutic alternative to continue to use LCV in the palliative treatment of this frequent disease.

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