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Rapid desensitization for L-asparaginase hypersensitivity

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L-asparaginase (LA), an active antileukemia agent, is often associated with allergic reactions. Intramuscular administration reduces the likelihood of severe allergic response. However, it is troublesome for patients with hemorrhagic diathesis, and up to 30% of children develop allergic reactions with intramuscular administration.¹ We report a case of successful intravenous desensitization for acute leukemia with anaphylaxis to LA.

A 2-year-old girl with acute myelogenous leukemia (FAB: M0) was first treated with a combination chemotherapy including LA at 13 months of age. The first chemotherapy course was well tolerated with intravenous administration of LA (10,000 U = 20,000 U/m²). Twenty minutes after initiation of LA in the second course, she had abrupt coughing and stridor and became dyspneic. Diffuse pruritic erythema and nasal discharge was also noted. Intravenous administration of LA was discontinued, and symptoms subsided within 1 hour with intravenous hydrocortisone and hydroxyzine. Four more courses were performed without LA, and the patient was kept in remission. After 2 months from the last chemotherapy, at 2 years of age, bone marrow relapse was noted. Reinstitution of LA was attempted intravenously because LA was still sensitive to the leukemic cells by in vitro assay, and the patient's platelet count was decreased. Intradermal skin tests with a commercial formulation of LA (JAN, INN; 9015-68-3; Kyowa Hakko, Tokyo, Japan) was positive at 5 U/ml. The desensitization protocol was designed to start with a 100-fold dilution of a minimal concentrate of positive skin test. The protocol is outlined in Table I, protocol 1. Each infusion bag was prepared in 5% dextrose and dripped in about 4 hours. All infusion bags were well tolerated without any adverse reactions. The patient completed two more courses in a similar manner without any adverse reactions. The patient was intravenously premedicated with hydroxyzine only in the first course. The fourth course was started with a concentrate of 0.2 U/ml because the intradermal skin test repeated after the third course showed a positive response at 50 U/ml and a negative response at 5 U/ml. The patient developed a rash with the last bag, but the

planned dose was completed with intravenous hydroxyzine. Three days later, a fifth course was attempted with a minor modification. After the first two bags, the infusion rate of the last infusion bag containing 4500 U of LA was gradually increased ([Table I, protocol 2](#)). No adverse effects were observed. The patient received three more LA courses with protocol 2, and no adverse effects were noted other than an occasional mild pruritus, which subsided with intravenous hydroxyzine.

Table I.

Protocol for LA desensitization

	Number of infusion bag	Concentration (U/ml)	Volume (ml)	Speed			Total dose (U)
				(U/hr)	(ml/hr)	Time (hr)	
Protocol 1	1	0.02	250	1.2	60	4.2	5
	2	0.2	225	12	60	3.8	50
	3	2	225	120	60	3.8	500
	4	20	225	1200	60	3.8	5000
Protocol 2	1	0.2	250	12	60	4.2	50
	2	2	225	120	60	3.8	500
	3	20	225	120	60	1	620
				240	12	1	860
				500	25	1	1360
				1000	50	3.6	5000

Protocol 1 was applied in the first four courses (4th course was started from 0.2 U/ml of concentration). Protocol 2 was applied in the rest of the courses.

The incidence of allergic reaction with LA is dependent on the biologic sources. *Escherichia coli*-derived LA was used in this patient, and as high as 45% of patients had allergic reactions with intravenous administration of this preparation ([Bonno et al., unpublished observation, 1995](#)). As described above, our protocol was well tolerated without any adverse effects. Previously, successful intravenous desensitization for antineoplastic agents was reported to carboplatin² and paclitaxel.³ Our experience suggests that intravenous desensitization to LA may also be safe and efficacious, especially for those with hemorrhagic [diathesis](#).

Motoki [Bonno](#), MD, Hajime Kawasaki, MD, Hiroki Hori, MD, Masakazu Umemoto, MD, Yoshihiro Komada, MD, Minoru Sakurai, MD, Department of Pediatrics, Mie University School of Medicine, 2-174, Edobashi, Tsu Mie 514 Japan

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