

Successful desensitization of elosulfase alfa–induced anaphylaxis in a pediatric patient with Morquio syndrome



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Clinical Implications

- In cases of severe hypersensitivity reactions such as anaphylaxis due to elosulfase alfa, desensitization can be applied to ensure the continuity of treatment. Our patient is the first case in the literature who was successfully desensitized against elosulfase alfa.

TO THE EDITOR:

Here, we present an 8.5-year-old girl who was diagnosed with Morquio syndrome in our pediatric metabolic disease clinic when she was 5 years old. She has been treated with 2 mg/kg dose of elosulfase alfa weekly in order to receive enzyme replacement therapy in the last year. Urticaria developed approximately 90 minutes after the initiation of infusion in the 28th, 29th, 30th, and 31st weeks of the treatment. The treatment was maintained by restarting the infusion after a cessation period and administration of antihistamines and systemic steroid. However, in the 32nd week of treatment, angioedema occurred on the eyelids and lips, and urticaria appeared on the trunk and extremities and was accompanied by shortness of breath, decrease in oxygen saturation, hypotension, and abdominal pain 30 minutes after the initiation of infusion. Thus, the infusion was discontinued and intramuscular adrenaline, antihistamines, and a systemic steroid were administered. Then, the patient was referred to our allergy clinic to be evaluated.

The skin tests were performed with the commercial preparation of the enzyme (Vimizim 5 mg/5 mL) to demonstrate the hypersensitivity of the patient. Skin prick test results with undiluted drug and intradermal test with 1/1000 dilution were negative. Intradermal test was repeated with 1/100 dilution; an 11 mm × 12 mm size endurance and surrounding erythema occurred and the test result was considered positive. In an attempt to eliminate false positivity, the drug was applied in 10 healthy people intradermally at the concentration of 1/100 and the results were negative. As a consequence, IgE-dependent allergy to the elosulfase alfa was confirmed in our patient. Because the treatment must be continued and there has been no alternative treatment, we decided to apply desensitization. In literature review, no desensitization protocol with elosulfase alfa was encountered. Therefore, we designed a new protocol as below.

Desensitization protocol: The total amount of enzyme that had to be received by the patient was calculated and accordingly 4 different bottles with the concentration of 1/1000, 1/100, 1/10, and 1/1 were prepared (Table I). This desensitization protocol with a total of 16 steps, 4 from each solution, was completed in 5 hours (Table II). Infusion was initiated 1 hour after the administration of antihistamine and antipyretic as pre-medication. Urticaria occurred in the 5th minute of the sixth step; thus, a second attempt was made 1 hour after the administration of 1 mg/kg of methylprednisolone. In this case, no reaction occurred and desensitization was completed successfully. By using this 16-step desensitization protocol, the patient has continued enzyme replacement therapy with elosulfase alfa every week without having any problems. To date the patient has received the enzyme 21 times without any reaction.

Mucopolysaccharidosis type IVA, also known as Morquio syndrome, is an autosomal-recessive inherited disease characterized by overaccumulation of keratan sulfate in lysosomes due to insufficient activity of *N*-acetylgalactosamine 6-sulfatase. The supportive treatment forms the basis of the management of this disease.^{1,2} Enzyme replacement is made with elosulfase alfa. Elosulfase alfa is a purified human enzyme produced by using the recombinant DNA technology.³ In the literature, it was noted that in 18.7% of patients treated with elosulfase alfa, hypersensitivity reaction develops in 30 minutes after the beginning of infusion, whereas in 6.8% of patients more severe reactions such as anaphylaxis were reported.⁴ In the case of severe hypersensitivity reactions such as anaphylaxis that was aroused because of the elosulfase alfa, desensitization can be applied to ensure the continuity of treatment. In the literature, no data exist regarding the desensitization of elosulfase alfa. Our patient is the first case who was successfully desensitized with the 16-step protocol. We suggest that the desensitization protocol can be used safely in similar cases. However, if 1 mg/kg of methylprednisolone is used as weekly pretreatment, surveillance and potential prophylaxis for corticosteroid side effects are required.

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TABLE I. Elosulfase alfa concentrations used to create desensitization protocol

Solution type	Solution content	Concentration
A	10 mL solution B + 90 mL 0.9% NaCl	0.15 µg/mL (1/1000)
B	10 mL solution C + 90 mL 0.9% NaCl	1.5 µg/mL (1/100)
C	10 mL solution D + 90 mL 0.9% NaCl	15 µg/mL (1/10)
D	30 mL drug* + 170 mL 0.9% NaCl	150 µg/mL (1/1)

NaCl, Sodium chloride.

*Elosulfase alfa (Vimizim) = 500 µg = 5 mL.

TABLE II. Intravenous desensitization protocol of elosulfase alfa

Step	Solution type	Rate (mL/h)	Infusion duration (min)	Volume infused per step (mL)	Dose administered with this step (µg)	Cumulative dose (µg)
1	A	4	15	1	0.15	0.15
2	A	8	15	2	0.3	0.45
3	A	16	15	4	0.6	1.05
4	A	32	15	8	1.2	2.25
5	B	8	15	2	3	5.25
6	B	16	15	4	6	11.25
7	B	32	15	8	12	23.25
8	B	64	15	16	36	59.25
9	C	16	15	4	60	119.25
10	C	32	15	8	120	239.25
11	C	64	15	16	240	479.25
12	C	128	15	32	480	959.25
13	D	24	15	6	900	1,859.25
14	D	48	15	12	1,800	3,659.25
15	D	96	15	24	3,600	7,259.25
16	D	120	75	150	227,40.75	30,000

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