



Letters

Successful desensitization to agalsidase beta after anaphylaxis

Fabry disease is a X-linked inherited lysosomal storage disorder caused by mutations of the *GLA* gene that results in an inborn deficiency of the enzyme α -galactosidase. Affected individuals include hemizygous males and heterozygous (carrier) females.¹ This deficiency results in the accumulation of globotriaosylceramide and other neutral glycolipids, which leads to cellular abnormalities and triggers inflammation and fibrosis of the skin, kidney, nervous system, and heart.¹ Life expectancy is approximately 50 years for males and 70 for females.^{2–5} Treatment includes enzyme replacement therapy with either agalsidase alfa or beta isozymes (A- β).

A- β is a foreign antigen to humans because it is produced in Chinese hamster ovary cells and undergoes nonhuman glycosylation. IgG antibodies to A- β are present in approximately 80% of untreated individuals, and IgE responses that result in anaphylaxis to A- β have been reported in 1% of individuals undergoing replacement therapy.^{6,7} A case of anaphylaxis to A- β followed by successful reintroduction after desensitization is presented.

A 50-year-old, white man with end-stage renal disease after cadaver kidney transplantation who is taking tacrolimus and mycophenolate mofetil developed A- β hypersensitivity 1 year after beginning intravenous A- β therapy. The patient was adherent to therapy and was receiving therapy once or twice a month, depending on the availability of the medication. He developed a pruritic, erythematous, maculopapular skin eruption on the torso and angioedema of the periorbital areas and lips during the infusion of 60 mg of A- β at 40 mL/h. Within a few minutes, he became hypotensive and was transferred to the intensive care unit. His signs and symptoms rapidly resolved with discontinuation of A- β therapy and administration of 0.3 mg of intramuscular epinephrine in the right deltoid, 50 mg of intramuscular diphenhydramine in the left deltoid, 125 mg of intravenous methylprednisolone, and 2 L of normal saline.

The patient was lost to follow-up for 8 months. Serum IgE and IgG test results to A- β were positive, and a baseline tryptase level measured during a visit at that time was normal. The result of a skin prick test (SPT) to A- β at 0.0014 mg/mL also was positive, with a wheal of 4 × 6 mm with no reaction to the negative control and 6 × 6 mm with histamine phosphate (0.1 mg/mL).

The patient was premedicated with 40 mg of oral prednisone at 12 hours and 20 mg at 4 hours before the procedure and then given incremental doses of A- β , a total of 35 mg (due to a shortage of A- β), to desensitize him (Fig 1). Intravenous diphenhydramine, 25 mg, and famotidine, 20 mg, were administered 20 minutes before beginning the procedure. Thereafter, he tolerated 35 mg of intravenous A- β once monthly using the same premedication and desensitization protocol.

However, 1 month later, using the same protocol, he developed generalized pruritus, rhinorrhea, and cough. The infusion was discontinued. Intravenous diphenhydramine, 25 mg, and

methylprednisolone, 125 mg, were administered with resolution of the symptoms. Subsequently, inpatient desensitization was accomplished to incremental intravenous doses of 3 mg of A- β using the same protocol as described above. Thereafter, a total of 2 intravenous doses of 35 mg and 1 intravenous dose of 60 mg, 2 weeks apart, were given using the same protocol before the patient was switched to outpatient infusion. In the outpatient infusion center, he was premedicated as described above and given 2 separate doses of 35 mg bimonthly without desensitization at 60 mL/h and thereafter prescribed bimonthly doses of 60 mg of intravenous A- β at 60 mL/h without premedication and desensitization.

The results of serum IgE tests and SPTs to A- β were positive in this patient, indicating that IgE mechanisms probably played a role in his anaphylaxis. A role for IgG cannot be excluded. Premedication and incremental dosing of A- β resulted in the successful desensitization and continuation of therapy. One additional report of 6 patients, with circulating IgE antibodies or SPT reactivity to A- β , also suggests that it is possible to reinstate A- β using an identical protocol.⁶ The 6 patients were administered lower doses at lower rates of infusion of A- β than that ordinarily used for routine care, and A- β was progressively titrated upward based on the individual patients' responses. However, unlike this reported case, premedication was used only after the first 4 successful infusions.

The advent of enzyme replacement therapy with recombinant human A- β is an important therapeutic option for patients with this progressive multisystem disorder. Clinical trials show improved outcomes if therapy with A- β is initiated before irreversible damage of vital organs occurs. Adverse reactions occur more commonly in patients IgG positive to recombinant A- β . However, the frequency and severity of adverse reactions are diminished by infusion rate optimization and the use of premedication possibly because of increased tolerance to the exogenous protein and decreasing antibody titers over time.^{6,7}

In conclusion, this study reports that premedication and desensitization to recombinant A- β in a patient with Fabry disease, who had previously experienced anaphylaxis to A- β , results in the successful reintroduction and continuation of the treatment.

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Target dose(mg):	35
Standard volume per bag(ml):	250
Final Rate of Infusion(ml/hr):	80
Calculated target concentration (mg/ml):	0.28
Standard time of infusion (minutes):	187.5

SOLUTION 1: 250 ml of 0.0014 mg/ml with a total of 0.35 mg per bag

SOLUTION 2: 250 ml of 0.014 mg/ml with a total of 3.5 mg per bag

SOLUTION 3: 250 ml of 0.1246 mg/ml with a total of 31.15 mg per bag

Step	Solution	Rate (ml/hr)	Time (min)	Volume infused per step(ml)	Dose administered with this step (mg)	Cumulative dose administered this step (mg)
1	1	2	15	0.5	0.0007	0.0007
2	1	5	15	1.25	0.0017	0.0024
3	1	10	15	2.50	0.0035	0.0059
4	1	20	15	5.00	0.0070	0.0129
5	2	5	15	1.25	0.0175	0.0304
6	2	10	15	2.50	0.0350	0.0654
7	2	20	15	5.00	0.0700	0.1354
8	2	40	15	10.00	0.1400	0.2754
9	3	10	15	2.00	0.3472	0.6226
10	3	20	15	5.00	0.6945	1.3171
11	3	40	15	10.00	1.3890	2.7061
12	3	80	15	232.50	32.2939	35.0000

Figure 1. Desensitization protocol for agalsidase beta.

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Spice allergies in children

Spice allergy is rare in children.¹ Saffron allergy in particular has been described only in adults²; it occurs generally in occupational

settings³ and is due to the Cro s 3 lipid transfer protein (LTP).⁴ We describe a case that is the exception to all these beliefs.

A 12-year-old boy followed up for allergic rhinitis to grass pollen, cat, and house dust mite also had oral allergy syndrome (OAS) and a positive skin prick test (SPT) result for apple, watermelon, and