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Drug Allergy in the Treatment of Mucopolysaccharidosis Type 1: A Case Study

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ABSTRACT

Mucopolysaccharidosis (MPS) is a group of progressive metabolic disorders (lysosomal storage diseases) characterized by the accumulation of glycosaminoglycans in various organs, including the skeletal system (dysostosis multiplex), viscera (hepatomegaly and splenomegaly), nervous system (neurological complications), eyes (corneal opacity and optic atrophy), and the cardiovascular system (valvular heart disease and cardiac thickening). The disease can be classified into several types based on the specific enzymatic deficiency. In some MPS types, treatment is administered weekly via enzyme replacement therapy. However, due to the risk of severe reactions, including anaphylaxis during infusion, these therapies must be given under close medical supervision. This article presents a case report of an 8-year-old girl diagnosed with Mucopolysaccharidosis type 1 (Hurler syndrome), who was treated weekly with two vials of Aldurazyme. The patient developed an allergy to this medication, which was successfully managed with a desensitization protocol. The protocol included premedication with prednisolone, lower dilutions of the drug, reduced infusion rates, and gradual increases in drug concentration and infusion speed, alongside routine enzyme administration.

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Introduction

Mucopolysaccharidosis (MPS) encompasses a group of progressive metabolic (lysosomal storage) diseases caused by deficiencies in enzymes essential for the metabolism of glycosaminoglycans. This condition is characterized by involvement of multiple organs, including the skeletal system (dysostosis multiplex), viscera (hepatomegaly and splenomegaly), nervous system (neurological complications), eyes (corneal opacity and optic atrophy), and cardiovascular system (cardiac thickening and valvular heart disease) [1-3]. The disease can be classified into different types based on the specific enzymatic deficiency [4,5]. Treatment approaches typically involve weekly enzyme replacement therapy; sometimes, hematopoietic stem cell transplantation may be considered [6]. If left untreated, MPS can lead to joint restrictions, reduced mobility, progressive cardiac complications, enlargement of abdominal organs, macroglossia, coarse facial features, upper airway obstruction, snoring, sleep apnea, respiratory issues, and, ultimately, death. Initiating enzyme replacement therapy halts disease progression, and timely treatment with appropriate dosing is critical for improving patient outcomes [7]. Patients with MPS often require enzyme replacement therapy, which may lead to side effects, including allergic reactions [8]. This article presents the case of a patient exhibiting drug hypersensitivity and outlines the desensitization protocol employed to manage this reaction.

Case Presentation

An 8-year-old girl diagnosed with Mucopolysaccharidosis type 1 (Hurler syndrome)

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was initially treated with two vials of Aldurazyme weekly. After two years, her dosage was increased to 3 vials due to weight gain. The patient then developed allergic reactions, including skin rashes, followed by abdominal pain and wheezing, which progressed to anaphylaxis. Initially, it was suspected that the infusion rate may have been too rapid, as the patient had received the medication at another hospital. However, at our center, the drug was administered under strict supervision, with premedication including antihistamines 30 minutes before infusion, and the medication started at a low dose according to protocol, with gradual increases in the infusion rate. Despite this careful approach, the patient continued to exhibit symptoms of anaphylaxis, suggesting an increased sensitivity to the medication. Consequently, a desensitization protocol was implemented.

Methods

According to standard protocols, enzyme administration requires pre-treatment before infusion. Following reports of drug reactions, patients should be observed either inpatient or outpatient. Before enzyme initiation, five cc of diphenhydramine or an antipyretic is administered 30 minutes before starting the enzyme, along with 1 mg of famotidine per kilogram of body weight. The enzyme is diluted in normal saline to a total volume of 100 cc and infused at an initial rate of 2 cc per hour. The infusion speed is doubled every 15 minutes until reaching 16 cc per hour, totaling about 4 hours. Given the patient's history of hypersensitivity and anaphylaxis, she was admitted to the pediatric intensive care unit. In addition to the standard pre-treatment, 1 mg of prednisolone per kilogram of body weight was administered 30 minutes before enzyme infusion. The enzyme infusion rate was gradually increased in 20 steps, starting with five solutions diluted at 1:10,000, 1:1,000, 1:100, 1:10, and the standard solution (as outlined in the protocol table). The patient received the enzyme in the intensive care unit during the first two admissions, beginning with a single vial. In subsequent admissions to the pediatric endocrine department, the standard dosage of 3 vials was infused over 24 hours, with infusion rates gradually approaching the standard rate. Over the next year, the drug was administered weekly without any reported severe reactions. After two months, prednisolone was gradually discontinued as pre-treatment before enzyme infusion, while famotidine and diphenhydramine were continued [9].

Step	Solution	Rate (ml/h)	Time (min)	Volume infused per step (ml)
1	1	1	15	0.25
2	1	2	15	0.5
3	1	4	15	1.00
4	1	8	15	2.00
5	2	2	15	0.5
6	2	5	15	1.25
7	2	10	15	2.5
8	2	20	15	5.00
9	3	1	15	0.25
10	3	2	15	0.5
11	3	4	15	1.00
12	3	8	15	2.00
13	4	2	15	0.5
14	4	5	15	1.25
15	4	10	15	2.5
16	4	20	15	5.00
17	5	5	15	1.25
18	5	10	15	2.5
19	5	20	15	5.00
20	5	39	100.4	65.25

Solution 1 (1/10,000): 100 ml; 0.0000087 mg/ml
Solution 2 (1/1,000):100 ml; 0.000087 mg/ml
Solution 3 (1/100): 100 ml; 0.00087 mg/ml
Solution 4 (1/10): 50 ml; 0.0087 mg/ml
Solution 5 (1/1): 100 ml; 0.087 mg/ml

Findings

During the desensitization protocol, the patient did not experience any severe reactions or anaphylaxis. She was able to continue enzyme therapy successfully, and the symptoms of the disease were gradually controlled. Final evaluations showed an improved overall condition and a positive response to treatment [10].

Discussion

The results of this study suggest that desensitization protocols can ensure the safety and efficacy of enzyme therapy in patients with a history of drug hypersensitivity. This highlights the need for further research to establish optimal practices and dosing regimens for desensitization.

Conclusion

Drug hypersensitivity in patients with mucopolysaccharidosis presents significant challenges; however, by implementing desensitization protocols, enzyme therapy can be continued, improving patients' quality of life.

Declaration

Authors' contributions

Specify each author's contributions to the manuscript.

Ethics approval and consent to participate

"Not applicable".

Consent for publication

"Not applicable."

Competing interests

"The authors declare no competing interests".

Availability of data and materials

You can request the study's data from the corresponding author.

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