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CASE REPORT

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Case series of desensitization to pegylated escherichia coli-derived asparaginase: An effective option in response to the need

Natalhie Acuña Ortega[a], Sandra N. González Díaz[a], Cindy E. De Lira Quezada[a], Ana K. Chávez Ruiz[a,*], Julia E. Colunga Pedraza[b], Danna S. Ríos González[a]

[a]*Regional Center for Allergy and Clinical Immunology, Dr. José Eleuterio González University Hospital, Autonomous University of Nuevo León, Monterrey, Mexico*
[b]*Department of Hematology, Dr. José Eleuterio González University Hospital, School of Medicine, Autonomous University of Nuevo León, Monterrey, Mexico and Francisco I. Madero Pte., s/n, and Gonzalitos Avenue, Colonia Mitras Centro, Monterrey, NL, Mexico*

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Abstract
Introduction: Asparaginase is an integral component in the treatment of acute lymphoblastic leukemia. The asparaginase products available in our country are Escherichia Coli (*E. Coli)*-derived asparaginase (Leunase), pegaspargase (Oncaspar), and, to a lesser extent, *Erwinia chrysanthemi*-derived asparaginase. Hypersensitivity reactions (HSR) are reported less frequently in those receiving pegaspargase, ranging from 3% to 15%; however, these reactions can limit its use in this population.
Case report: We present four patients with B-cell ALL who experienced a severe allergic HSR, anaphylaxis, leading us to perform a 12-step desensitization protocol to pegaspargase to ensure that the patients received first-line treatment for their oncologic condition.
Management and outcomes: Skin tests were performed, with positive results in two out of four patients. Subsequently, a 12-step desensitization protocol was carried out. Pegaspargase was diluted with 0.9% saline solution in three bags (concentrations 1:100, 1:10, and 1:1). Infusions used four steps per bag titrated every 15 minutes up to a maximum rate of 80 mL/hour for step 12. A successful administration of pegaspargase was achieved, and the patients continued with their ALL treatment.
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***Corresponding author**: Ana Karen Chávez Ruiz MD, Regional Center for Allergy and Clinical Immunology, Dr. José Eleuterio González University Hospital, Autonomous University of Nuevo León, Monterrey, Mexico. *Email address*: anakaren_ch93@hotmail.com

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Introduction

Asparaginase is used as part of the treatment for acute lymphoblastic leukemia (ALL) and non-Hodgkin lymphoma. It takes advantage of the lack of asparagine synthesis in lymphoid blasts until asparagine is depleted.[1] Several types of asparaginases with the same mechanism of action are available on the market. These include native preparations derived from *Escherichia coli* (*E. Coli)* (L-ASP) and *Erwinia chrysanthemi*, chemically modified preparations of E. coli asparaginase conjugated with polyethylene glycol (PEG-ASP), recombinant preparations of *E. coli*-derived asparaginases, and a recombinant *Erwinia* asparaginase derived from *Pseudomonas fluorescens*.[2]

Exposure to asparaginase, a foreign protein, can lead to the development of anti-asparaginase antibodies.[3] Hence, one of the most common adverse effects in asparaginase treatment are hypersensitivity reactions (HSRs), which range from localized erythema and urticaria to anaphylaxis.[2,3] HSR can occur from the first dose of asparaginase, but the risk increases with repeated administrations, especially during consolidation and reinduction treatment phases.[4,5]

PEGylation, the conjugation of drugs with polyethylene glycol (PEG), is widely used in recent drug development. PEGylated drugs have longer half-lives and are less immunogenic. PEG-ASP is replacing native *E. coli* L-ASP in ALL treatment regimens, as it causes less hypersensitivity. However, reactions to PEG-ASP are not uncommon.[1] HSR are generally reported in 10% to 30% of patients receiving L-ASP, less frequently in patients receiving PEG-ASP from 3% to 15% (a rate that can be reduced from 4% to 5% using premedication during initial therapy),[6] and from 3% to 37% in patients receiving *Erwinia* asparaginase.[1,2]

HSRs are problematic because they cause morbidity and inadequate asparaginase activity, requiring a switch to *Erwinia* asparaginase, a formulation that requires frequent administration at a high cost.[1,6] It is increasingly recognized that PEG itself can act as an allergen, but its contributions to reactions to PEG-ASP remain poorly characterized, such as the risk factors for PEG-ASP allergy.[7,8]

Another important point to consider is that in some countries, *Erwinia*-derived asparaginase is not available. Therefore, desensitization to any form of *E. coli*-derived asparaginase becomes a better therapeutic option, allowing patients with HSRs to these drugs to maintain treatment administration.[7] However, there is limited experience reported with desensitization to PEG-ASP.[7]

Case Report

Because of the scarcity of *Erwinia* asparaginase in our hospital and the need to provide effective treatment, a rapid desensitization protocol was performed on four patients with a history of severe allergic reactions to PEG-ASP. Patients/guardians provided informed consent and patient assent in accordance with the Declaration of Helsinki. All research was approved by the institutional review board.

Patients were assessed in the allergy department where a prick test was performed with undiluted PEG-ASP; all four patients showed negative results, so an intradermal test was performed at a concentration of 20 U/mL,[9] resulting in two patients with positive and two with negative results.

The total dose was calculated based on each patient's body surface area. A 12-step desensitization protocol was used (Table 1). PEG-ASP was diluted with 0.9% saline solution in three bags (concentrations 1:100, 1:10, and 1:1). Infusions used four steps per bag titrated every 15 minutes up to a maximum rate of 80 mL/hour for step 12. Premedication with cetirizine, aspirin, montelukast, hydrocortisone, and ondansetron was given 30 minutes before desensitization. All patients were monitored during the procedure.

Conclusions

In this case series, a total of 13 desensitizations to PEG-ASP were performed. The characteristics of the four desensitized patients are described in Table 2. The mean time from PEG-ASP administration to the initial reaction was 15 minutes. All infusions were successfully completed.

During desensitizations, skin symptoms were observed in patient 2; the infusion was stopped, and intravenous fluids and a new dose of cetirizine, montelukast, and hydrocortisone were administered. For the next administration to this patient, premedication with cetirizine, aspirin, and

Table 1 Rapid desensitization protocol to pegylated Escherichia Coli asparaginase (PEG-ASP).

Total dose	750 UI	Dilution concentration (UI/mL)	Total dose of each dilution (UI)
Dilution A (1:100)	7.5 UI	0.03	0.28
Dilution B (1:10)	75 UI	0.3	5.6
Dilución C (total dose)	744.12 UI	2.9	744.12
Step	**Solution**	**Infusion mL/h**	**Duration (min)**
1	A	2.5	15
2	A	5	15
3	A	10	15
4	A	20	15
5	B	5	15
6	B	10	15
7	B	20	15
8	B	40	15
9	C	10	15
10	C	20	15
11	C	40	15
12	C	80	174.4

Example of patient number 4 requiring 750 IU of PEG-ASP. The total duration is approximately 5 hours and 45 minutes to 6 hours.

Table 2 Patient Characteristics.

Patient	1	2	3	4
Age	9	22	7	6
Sex	M	M	F	M
History of atopy	Allergic rhinitis and asthma	Denied	Allergic rhinitis	Denied
Symptoms of the initial PEG-ASP reaction	Palate itch, hives, wheals, sensation of shortness of breath, and chest tightness.	Hypotension, oxygen desaturation, throat sensation of foreign body, hives, abdominal colic, and nausea.	Tachycardia, oxygen desaturation, generalized urticaria with predominance on face and upper limbs, abdominal pain, vomiting, and lumbalgia.	Tachycardia, generalized redness and itching, abdominal pain, nausea, and vomiting.
Brown scale severity level of HSR	2	3	3	2
Ramon y Cajal scale severity level of HSR	3	4	3	3
Initial premedication in the initial reaction	Hydrocortisone, diphenhydramine, ondansetron	Hydrocortisone, chlorphenamine, ondansetron	Hydrocortisone, diphenhydramine, ondansetron	Dexamethasone, diphenhydramine, ondansetron
Number of administrations when the initial HSR occurred	3	1	2	2
Time elapsed from administration to initial HSR occurrence	15–30 minutes	15–20 minutes	15–30 minutes	5–15 minutes
Prick test result	Negative	Positive	Negative	Positive
Number of desensitizations	3	2	3	5
Premedication for desensitization	Hydrocortisone, montelukast, and cetirizine.	Hydrocortisone, aspirin, montelukast and cetirizine.	Hydrocortisone, aspirin, montelukast, and cetirizine.	Hydrocortisone, aspirin, montelukast and cetirizine
Symptoms during desensitization	No	Redness and itching in the upper trunk.	During the last administration, she developed generalized urticaria, abdominal pain, and vomiting (the patient also had gastroenteritis as a cofactor).	No
Treatment provided for symptoms experienced during desensitization	NA	Cetirizine, montelukast, hydrocortisone, and IV fluids. Premedication was given 3 days before for the following desensitizations*.	IM epinephrine, cetirizine, montelukast, aspirin, ondansetron, hydrocortisone, and IV fluids.	NA

HSR: hypersensitivity reaction; PEG-ASP: polyethylene glycol-conjugated *Escherichia Coli* asparaginase; NA: not applicable. *In patient 2, premedication was initiated from the first desensitization (after experiencing symptoms during the procedure), 72 hours before the procedure with cetirizine, aspirin, and montelukast, and on desensitization day, hydrocortisone and ondansetron were additionally administered to the aforementioned premedication.

montelukast was given 3 days before, and no reactions occurred during the procedure. On the other hand, patient 3 presented anaphylaxis during the third desensitization, suspected to be favored by an infectious process at that time (infectious gastroenteritis), as a cofactor. The desensitization was suspended, and the patient was scheduled for completion the next day. This second attempt was completed without complications. This patient has not been desensitized again, as she entered an intensification regimen.

Prick tests are useful in type I IgE-mediated HSRs; however, it has been described that the HSR developed by patients treated with PEG-ASP may be because of IgG, IgE, and IgM antibodies against PEG-ASP and PEG itself.[2,3] This explains why, in spite all four patients developing clinical manifestations of HSR, only two tested positive in the tests performed. It is likely that the other two patients had an HSR mediated by IgG or IgM antibodies. It would be useful to conduct more studies to characterize our population and determine the presence of IgG and IgM antibodies against PEG-ASP and PEG, and to investigate whether these antibodies are useful biomarkers for predicting success or failure in achieving desensitization, as well as whether their levels decrease or increase with each desensitization performed.

Another growing concern in PEG-ASP treatment is determining the optimal asparaginase activity during treatment, as desensitized patients with antibodies are at risk of rapid PEG-ASP elimination and may have inadequate asparaginase activity after desensitization.[1] Rizzari et al. demonstrated that minimum asparaginase activity levels <0.05 IU/mL, obtained with native *E. coli* or *Erwinia* asparaginase, resulted in asparagine serum and cerebrospinal fluid depletion in children with ALL.[3]

In a study of patients with ALL and HSR to PEG-ASP who underwent desensitization, Swanson et al. reported successful treatment rates in seven patients who completed the infusion and six maintaining asparaginase activity of at least 0.1 IU/mL for 14 days, thus demonstrating the feasibility of desensitization to PEG-ASP in patients with persistent anti-PEG-ASP antibodies. Furthermore, these antibodies were negative in three cases at the end of desensitizations.[7] In our patients, asparaginase activity was not quantified; however, a favorable response was observed as patients progressed in ALL treatment. Patients 1, 2, and 4 are already in the maintenance phase without relapses, and patient 3 remains in intensification.

Discussion

We report this series of four patients to whom we performed a total of 13 successful desensitizations, ensuring they continued their ALL treatment. More studies are needed to determine the type of antibody developed by our population against PEG-ASP, to discover if the type of antibody (IgG, IgM, IgE against PEG-ASP or PEG) is related to the severity of HSR and its subsequent negativization during desensitizations, and, finally, to determine the asparaginase activity in patients with HSR who undergo desensitization.

Mandatory Disclosure on Use of Artificial Intelligence

The authors declare that no AI-assisted tools were used in the preparation of this manuscript. All references have been manually verified for accuracy and relevance.

Author Contributions

All authors contributed equally to this article.

Conflicts of Interests

The authors had no relevant financial interests to disclose.

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References

1. Liu Y, Smith CA, Panetta JC, Yang W, Thompson LE, Counts JP, et al. Antibodies predict pegaspargase allergic reactions and failure of rechallenge. J. Clin. Oncol. 2019;37:2051–61. https://doi.org/10.1200/JCO.18.02439
2. Burke MJ, Zalewska-Szewczyk B. Hypersensitivity reactions to asparaginase therapy in acute lymphoblastic leukemia: immunology and clinical consequences. Future Oncol. 2022;18:1285–99. https://doi.org/10.2217/fon-2021-1288
3. van der Sluis IM, Vrooman LM, Pieters R, Baruchel A, Escherich G, Goulden N, et al. Consensus expert recommendations for identification and management of asparaginase hypersensitivity and silent inactivation. Haematologica. 2016;101:279–85. https://doi.org/10.3324/haematol.2015.137380
4. Rizzari C, Conter V, Starý J, Colombini A, Moericke A, Schrappe M. Optimizing asparaginase therapy for acute lymphoblastic leukemia. Curr. Opin. Oncol. 2013;25 (Suppl 1):S1–9. https://doi.org/10.1097/CCO.0b013e32835d7d85
5. Pagani M, Bavbek S, Alvarez-Cuesta E, Berna Dursun A, Bonadonna P, Castells M, et al. Hypersensitivity reactions to chemotherapy: an EAACI position paper. Allergy 2022;77:388–403. https://doi.org/10.1111/all.15113
6. Broyles AD, Banerji A, Barmettler S, Biggs CM, Blumenthal K, Brennan PJ, et al. Practical guidance for the evaluation and management of drug hypersensitivity: specific drugs. J Allergy Clin Immunol Pract. 2020;8(9):S16–S116. https://doi.org/10.1016/j.jaip.2020.08.006
7. Swanson HD, Panetta JC, Barker PJ, Liu Y, Inaba H, Relling MV, et al. Predicting success of desensitization after pegaspargase allergy. Blood 2020;135:71–5. https://doi.org/10.1182/blood.2019003407
8. Broos N, Brigitha LJ, Schuurhof A, Röckmann-Helmbach H, Tissing WJE, Pieters R, et al. Safety of mRNA-based COVID-19 vaccination in paediatric patients with a PEG-asparaginase allergy. EJC Paediatr. Oncol. 2023;1:100002. https://doi.org/10.1016/j.ejcped.2022.100002
9. Turgay Yagmur I, Guzelkucuk Z, Yarali N, Ozyoruk D, Toyran M, Civelek E, et al. Evaluation of hypersensitivity reactions to cancer chemotherapeutic agents in pediatric patients. Ann. Allergy Asthma Immunol. 2020;124:350–6. https://doi.org/10.1016/j.anai.2020.01.010