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Case Report

Liposomal Amphotericin B Successful Desensitization Protocol for the Treatment of Aspergillosis in Immunocompromised Woman: Case Report

Alandijani SA[1], Mohamed Abdilahi[2], Alariefy MA[3]*, Almutairi TN[3] and Alghanemi MG[4]

[1]Depatment of immunology, King Faisal Specialist Hospital, Saudi Arabia

[2]Pharmaceutical Care Division, King Faisal Specialist Hospital, Saudi Arabia

[3]University of Jeddah, Saudi Arabia

[4]King Abdulaziz University, Saudi Arabia

***Corresponding author:** Mohammed Abdullah Alariefy, University of Jeddah, Saudi Arabia

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Abstract

Drug allergies presents a major obstacle in the management of diseases, especially when the alternative drug is not available. liposomal amphotericin B anaphylaxis is rare and it's clinical significance lays in the idea that often there's is no alternative use. A 22-year-old female, known case to have pre-B cell acute lymphoblastic leukemia, status post allogenic bone marrow transplant. Admitted to the ICU with respiratory failure secondary to either drug induced, Graft versus host disease or bacterial vs fungal infection. The patient started to have a reaction from Amphotericin B which manifested as lip swelling and shortness of breath as well. A 12-step protocol of liposomal amphotericin B desensitization was created. She has tolerated this regimen and has had no recurrence of lip swelling and shortness of breath or any adverse reactions.

Keywords: Anaphylaxis; Drug; Allergy; Liposomal Amphotericin B; Desensitization

Introduction

Desensitization is defined as drug tolerance and decrease allergic response to medication.

Amphotericin B is an anti-fungal treatment against wide variety of a mold, yeast and *Leishmania* spp. It works through binding to ergo sterol in the cell membrane of the fungus and form pores that will lead to Na, K, H and Cl ions leakage and eventually, cell death. The precise mechanisms of transfer from liposome to fungal membrane is not well understood but high affinity of Amphotericin B to fungus sterol and body temperature may have rule [1]. Amphotericin B considered as second drug of choice after Voriconazole in treating invasive aspergillosis. Historically, it was discovered in (1950s), the formulation named as amphotericin B deoxycholate (DAmB). For many decades, DAmB solely treated invasive fungal diseases. However, the infusion related reactions and nephrotoxicity of the medication shed a light to develop a new form of the drug, a less toxic formulation [1,2]. Liposomal amphotericin B was introduced with a trade name of (AmBisome®; LAmB). It has been used for almost 20 years to treat broad spectrum of fungal infections. Its toxicity is significantly reduced while retaining its antifungal activity [3]. Nevertheless, Amphotericin B has been reported to cause shortness of breath, swelling of the lips and anaphylaxis like picture. Indeed, the drug eruption disappeared after discontinuation of the Amphotericin B and reappeared after the drug was reintroduced [4,5]. The mechanism of reaction is due to liposome rather than Amphotericin B even though the immediate reaction it's mainly complement mediated and not IgE mediated [6]. This case describes a life-threatening anaphylaxis while the patient is receiving Amphotericin B. Subsequently she underwent a successful desensitization to this medication.

Case Report

A 22-year-old female, known to have pre-B cell acute lymphoblastic leukemia, she underwent a successful allogenic bone marrow transplant. Admitted to the critical care unit with respiratory failure secondary to either drug induced, Graft versus host disease or bacterial Vs fungal infection. The patient started on treatment with liposomal Amphotericin B for positive bilateral lung infiltrate, which is thought to be due to fungal infection due to her impairment in immune status. The patient started to have a reaction from Amphotericin B in the second course after completion of the half of the dose which manifested as lip swelling and shortness of breath as well. Amphotericin B was stopped and switched to IV Voriconazole. However, due to her increased liver enzymes, Amphotericin B was the choice for her. Therefore, the decision that the patient should undergo Amphotericin B desensitization was done. An informed consent from the patient was taken. The plan was discussed with primary team and the infectious team. A slow tapper of 12 steps which is outlined in Table 1 desensitization protocol was started. The desensitization protocol was uncomplicated, and the patient started to have the full dose at the end of the protocol. She has tolerated this regimen and has had no recurrence of lip swelling and shortness of breath or any adverse reactions.

The protocol composed of 12 steps, the target is to reach 250mg Amphotericin B with infusion rate of 80ml/hr and dividing each 4 steps with a single solutions starting from solution 1 of 250ml with Amphotericin B concentration of 0.01mg/ml which equal 2.5mg per

Table 1: Amphotericin B desensitization schedule.

	Standard volume per bag (ml)	Drug concentration (mg/ml)
Solution 1	250 ml	0.01 mg/ml
Solution 2	250 ml	0.1 mg/ml
Solution 3	250 ml	1 mg/ml
	Target dose (mg)	250 mg

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Step	Solution	Rate (ml/hr)	Time (min)	Volume infused per step (ml)	Dose administered with this step (mg)	Cumulative dose (mg)
1	1	2	15	0.5	0.005	0.005
2	1	5	15	1.25	0.0125	0.0175
3	1	10	15	2.5	0.025	0.0425
4	1	20	15	5	0.05	0.0925
5	2	5	15	1.25	0.125	0.2175
6	2	10	15	2.5	0.25	0.4675
7	2	20	15	5	0.5	0.9675
8	2	40	15	10	1	1.9675
9	3	10	15	2.5	2.5	4.4675
10	3	20	15	5	5.0	9.4675
11	3	40	15	10	10.0	19.4675
12	3	80	172.9	230.5333333	230.5333333	250
		Total time (minutes) =	337.9	Total time (hours) =	5.631666667	

bag with infusion rate of 2ml/hr and up escalating the dose and the rate to finally reach to target dose of Amphotericin B as it's shown in Table 1.

Discussion

Amphotericin B is considered to be an effective drug against systemic fungal infection such as Candida species, Aspergillus species and/or Cryptococcus species infections. It also can be beneficial and less harmful in patients with hepatic impairment than Voriconazole. Although, Amphotericin B can cause an anaphylactic attack such as shortness of breath and swelling of the lips as it happened to our case here. Due to highly suspicion of Aspergillosis pneumonia in this case, we started with the aspergillosis management. The initial outline management of Aspergillosis is to start by Voriconazole treatment. However, Because of her hepatic impairment, Amphotericin B has chosen as a substitutional therapy as it's considered to be a second line therapy. Although, she subsequently developed allergic symptoms after introducing Amphotericin B. So desensitization attempt was required here. To our knowledge, this is the first report of a desensitization procedure for an IgE mediated reaction that occurred subsequent to Amphotericin B administration especially in Saudi Arabia. In this case, we followed the

standardized 12-step Desensitization protocol that has been used with various drugs such as some antibiotics. We followed the sensitization to some antibiotics in CF patients with hypersensitivity towards certain Antibiotics. They have considered it safe as they followed the 12-step desensitization protocol. Only 13.4% developed adverse reaction and most of them were mild [7]. We followed a safe protocol regarding the desensitization of Amphotericin B while putting the patient's conditions and comorbidities as well as other possible options in consideration and it turns out to be successful. In conclusion, our report suggests that it's safe to develop or use a desensitization protocol for patient with Ige mediated reactions to Liposomal Amphotericin B.

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