

Hypersensitivity reactions to Liposomal Amphotericin in a bone marrow transplant patient

Alaa Alsajri¹, Shadan Al-Hishma², and Mazin Shubber³

¹Affiliation not available

²Specialized Bone Marrow Transplant Center

³Specialized Bone Marrow Transplant Center

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Abstract

Introduction: Hodgkin's lymphoma is one of the treatable types of blood cancer. Autologous bone marrow transplantation is used as one way to treat this disease. Neutropenic fevers are treated with antibiotics and antifungals; including amphotericin B. Adverse effects and hypersensitivity to Liposomal Amphotericin, Ambisome, are very few compared to conventional amphotericin. **Case report:** In this case, we noticed hypersensitivity reactions to the Ambisome, represented by an increase in body temperature, a drop in blood pressure, hypo-oxygenemia, in addition to an increase in the heart rate. **Case management:** The patient was treated with injections of hydrocortisone, Chlorpheniramine, and normal saline, in addition to giving oxygen, he is improved. **Conclusion:** In spite of the few cases that have recorded hypersensitivity reactions to the Ambisome, it is necessary to conduct an allergy test and to monitor the patient well when giving the Ambisome, especially in the first dose.

Introduction

Bone marrow transplant, known as hematopoietic stem cells transplant (HSCT), entails infusion of healthy hematopoietic stem cells into patients with diminished or dysfunctional bone marrow. This aims to boost bone marrow function and allows to either destroy tumor cells with malignancy or to generate functional cells that can replace the dysfunctional cells[1]. It can be used in various types of diseases including leukemia, lymphoproliferative disorders, solid tumor, non-malignant disorders, and others[2]. Life enhancing HSCT is mainly divided into two main types, the autologous form (stem cells are harvested from the recipient) and the allogeneic form (stem cells are harvested from a different donor individual or from cord blood units)[3].

Our bone marrow transplant center is at the medical city, Baghdad we commonly use autologous stem cell transplant as a mainstay treatment line for patients with relapsed Hodgkin lymphoma, moderate-high degree non-Hodgkin lymphoma, and multiple myeloma after the failure of therapy with chemotherapy alone or in combination with radiotherapy. Patients who undergo bone marrow transplantation procedures are at high risk of severe illness, infectious complications, and myelosuppression including neutropenia[4].

Patients with Low neutrophil count (less than $500/\mu\text{L}$) and febrile, 38°C that consist for one hour or 38.3°C for one reading, few days after transplantation have febrile neutropenia which considered as a medical emergency. It may represent the only clinical sign of severe infection leading to increased length of hospital admission and prompts the physician to initiate empirical broad spectrum antimicrobial therapy prior to isolation of bacterial organism. Early administration of antimicrobial will improve overall morbidity and mortality rates[5, 6]. Choosing appropriate empirical therapy is a raising challenge especially in an era of elevated antimicrobial resistance rates[7]. Unresponsiveness with persistent or recurrent fever despite of antibiotic therapy could indicate an invasive fungal infection that requires the administration of empirical antifungal therapy because Invasive fungal infection risk increases with neutropenia duration and severity[8,

9]. Amphotericin B deoxycholate (conventional) for many decades is believed to be a cornerstone treatment of fungal infection [10]. Unfortunately, empirical treatment with conventional amphotericin B is limited by breakthrough fungal infections, acute toxic effects related to the infusion, and dose-limiting nephrotoxic reactions[11]. An alternative strategy that improves outcomes like evaluating lipid formulations of amphotericin to enhance tolerability profile conventionally has demonstrated significant benefits in treating fungal infections like liposomal amphotericin B[12]. In our BMT center, we started to administer liposomal amphotericin which is a unique lipid formulation of amphotericin B. used for a wide range of medically fungal pathogens. It has significantly improved safety and toxicity profile compared with conventional amphotericin B deoxycholate[13, 14].

Case details

An 18-year-old man diagnosed with Hodgkin’s lymphoma was admitted to the Specialized Center for Bone Marrow Transplantation for autologous stem cell transplantation.

The LEAM (Lomustine, Cytarabine, Etoposide, and Melphalan) therapeutic protocol was used as a conditioning regimen before stem cell transplantation according to the National Health Service (NHS) protocol[15].

Three days after stem cell transplantation (day +4), the patient entered a state of low neutrophil count, which was equal to (35) μl . On the next day (day +3), the patient’s temperature elevated to 38°C , which was considered as neutropenic fever. The doctor began dispensing antibiotics to the patient, such as Piperacillin+Tazobactam, and then Meropenem, but the temperature did not decrease. The doctor added Vancomycin treatment in order to cover the gram-positive bacteria, then he added Amikacin, but to no benefit. On the eighth day after the cell transplantation (day +9), the doctor added the liposomal Amphotericin (Ambisome) therapy in order to control the neutropenic fever. The dose of Ambisome) was calculated on the basis of the patient’s weight[11], which was compromising 70 kg, 210 mg of Ambisome in 500 ml of glucose-water 5% (D5W) infused over two hours. As a liposomal amphotericin is safer than conventional amphotericin, The treatment of Ambisome was given without sensitivity test or the addition of hydrocortisone and Chlorpheniramine before it[16].

After completing the infusion of the Ambisome, the patient suffering from skin rash, redness and chills accompanied by elevation in body temperature, increase pulse rate, a drop in blood pressure, and a decrease in the percentage of blood saturation with oxygen, as shown in the **table 1** . In order to ascertain the possibility that the drug is the cause of hypersensitivity, the Naranjo score was calculated and it was equal to (5). This indicates that the drug caused the hypersensitivity reaction[17].

The physicians prescribe hydrocortisone vial 100 mg plus chlorpheniramine ampoule, Normal saline 0.9% and Oxygen therapy to manage patient sever allergy. After the rapid intervention, the patient’s condition was clinically stable.

Discussion

Hodgkin’s lymphoma is a type of blood cancer that responds to treatment. This type of disease is considered uncommon. Chemotherapy is the first line in controlling this disease. In the advanced stages of the disease and in recurrent cases, a bone marrow transplant may be performed to control the disease[18].

In general, marrow transplantation is divided into two main types according to the source of stem cells, which are autologous bone marrow transplantation where stem cells from patient and allogeneic bone marrow transplantation, from a donor. There are many chemotherapeutic protocols prior to marrow transplantation, in order to prepare the bone to receive stem cells. These chemical protocols are in high doses and cause many complications, including neutropenia and neutropenic fever[19].

One of the treatments used in the treatment of neutropenic fever is the liposomal Amphotericin-B (Ambisome)[10].

A hypersensitivity reaction to liposomal Amphotericin has been reported in many cases [20-24]. This is the first case to report hypersensitivity to liposomal Amphotericin-B (Ambisome) in patients with bone

marrow transplantation in bone marrow transplant center, Iraq. The allergy occurred from the first dose that was given to the patient, and the situation was corrected by giving some medications that reduced the sensitivity and improved the patient's condition. Although this is the first case of an allergic reaction to liposomal Amphotericin-B recorded in our center, great care must be taken in patients who take Liposomal Amphotericin-B, especially in the first dose.

The approval of the bone marrow transplant center and the patient was obtained in order to publish this data and study.

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Table1 : vital signs before, at end of infusion and after Ambisome administration

Vital signs	Before Ambisome 12:00 pm	At the end of Ambisome infusion 02:00 pm	After allergy management 03:00 pm
Body temperature	36.1°C	39°C	36.3°C
O2 saturation	100%	65%	99%
Blood pressure	114/64	102/43	108/54
Respiratory rate	20	22	18
Pulse rate	107	133	106