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A CASE REPORT ON LIPOSOMAL AMPHOTERICIN- B INDUCED ANAPHYLACTIC REACTION

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Abstract:

Liposomal amphotericin-B is universally used antifungal drug for treatments of invasive fungal infections. The liposomal amphotericin-B is used extensively in medical setting because of its tolerability and potent antifungal activity. Allergic reaction to liposomal amphotericin B is infrequent. We report a case of anaphylactic reaction in a 57-year-old man following liposomal amphotericin B infusion. The patient was managed with immediate action of intravenous Noradrenaline, Ondansetron, Pheniramine and Hydrocortisone.

Key Words: Liposomal Amphotericin-B, Anaphylactic Reaction, Post covid Mucormycosis

INTRODUCTION:

COVID-19 impacted India severely, especially during the second wave. India, with a population of more than 1.34 billion, experienced significant problem in controlling the transmission of COVID-19 infection among its population [(1)]. As the conflict against the deadly Covid-19 epidemic is continuing worldwide, several complications are being reported in cases who have recovered post-covid. A fungal disease called Mucormycosis is one of the fatal complications being reported in patients in India, who have tested positive for Covid-19 and with gradual recuperation. Mucormycosis, also known as 'black fungus', is a fungal infection caused by the mucormycetes family of moulds, which are ubiquitous, commonly found in soil and decaying matter [(2)]. Post-Covid-19 patients who are more vulnerable to Mucormycosis are those with a history of inadequately uncontrolled diabetes mellitus and also those who are immune-compromised and have been treated with steroids and other medicines for Covid-19. When mucormycosis is suspected, appropriate imaging to document the extent of the disease is firmly advised, followed by surgical debridement of the affected area. Amphotericin B is suggested as a first-line treatment, whereas intravenous isavuconazole and intravenous or delayed-release-tablet posaconazole have also been recommended [(3)]. Amphotericin B is a low-soluble polyene antibiotic which has the property to self-aggregate. Activity and pharmacokinetics characteristics can be modified by its aggregated state. Despite of its high adverse effects it is still extensively used for the treatment of systemic fungal infections and parasitic disease and different formulations are marketed. The antifungal-activity of amphotericin B depends mainly by its ability to bind ergosterol in the cell membrane of susceptible fungi. This creates a transmembrane channel, and the resultant change in membrane permeability allowing leakage of intracellular components leading to loss of membrane integrity. Four formulations of amphotericin B marketed are conventional amphotericin B, amphotericin B colloid dispersion, liposomal amphotericin B, and amphotericin B lipid complex [(4)].

CASE PRESENTATION:

A 57-year-old male patient with no known drug allergies was admitted with post covid fronto ethmoidal mucormycosis, he had undergone endoscopic debridement before a month at another hospital. His swelling over the nasal bridge area was gradually increasing so he came to our hospital for further management. He has the past history of type two diabetes mellitus for 20 years and on treatment. His MRI brain, MRV and MRA was suggestive of mid frontal lesion extending into the frontal air sinus and extradural extension. These were the evidence of thrombus of the anterior third, superior sagittal sinus. A CT- Brain was performed and it indicated Fronto ethmoidal mucormycosis. Initially he was treated with anticonvulsant Levetiracetam 500mg BD orally and Analgesics Ketorolac 15mg BD and Tramadol 100mg BD intravenously. He was prescribed with Antifungal Amphotericin B lipid emulsion 5mg / kg infused over 4 hours. He was normotensive before starting the infusion. Thirty minutes after the infusion was initiated, the patient complained of chills, fever (temperature 37.6^{o}C) and nausea which was treated with Ondansetron 4mg IV and Paracetamol 1mg IV. Infusion was stopped due to the intolerance of the patient. The drug was readministered after 8 hours with the premedication of Ondansetron 4mg and Paracetamol 1g. Twenty minutes after initiating the infusion the patient developed severe hypotension (80/40mmhg), respiratory distress, fever and rigor. He was shifted to Intensive Care Unit and put on NIV mask. Amphotericin infusion was discontinued. He was immediately treated with intravenous Noradrenaline infusion (14ml/hr), Hydrocortisone 100mg, Pheneramine and Ondansetron 4mg. His condition improved in 12 hours. After a week patient underwent debridement surgery and prescribed with oral posaconazole.

DISCUSSION:

Amphotericin B is available in four different formulations as the plain drug, a cholesteryl sulfate complex, a lipid complex and as a liposomal preparation. The latter three formulations were developed to improve tolerability for the patient [(6)]. Liposomal Amphotericin-B alters its pharmacokinetics, and is associated with fewer nephrotoxic and infusion-related adverse effects than conventional amphotericin B (amphotericin B desoxycholate)[(7)] The liposome creates a closed, spherical vesicle around the Amphotericin B molecules, which allows it to change its pharmacokinetics to decrease the toxic reaction by facilitating targeted administration of the Amphotericin B by binding to the fungal cell walls, while at the same time protecting human cells from exposure to Amphotericin B [(8)] . Liposomes and lipid excipient-based drugs are generally recognized by the immune system as foreign, resulting in a variety of adverse immune phenomena. One of them is complement activation, the cause, or major contributing factor to, an anaphylactic reaction [(5)]. In a large series of patients treated with Amphotericin lipid complex were present with fever and chills, however these symptoms were usually mild, and discontinuation of the drug was not necessary [(9)]. Severe reactions to Liposomal Amphotericin-B, including anaphylaxis, are uncommon. The above discussed case shows the anaphylactic reaction developed during the infusion of liposomal Amphotericin-B. The occurrence allergic reactions to liposomal Amphotericin B during the treatment of mucormycosis warrants close supervision of patient, particularly since Amphotericin is currently first-line treatment for mucormycosis. Amphotericin-B should be administered under close observation. The use of prophylactic premedication and test dose administration of Amphotericin-B can be considered.

CONCLUSION:

The present case report shows the anaphylactic reaction caused by the Amphotericin-B infusion. The use of Liposomal Amphotericin-B is increasing in medical setting because of its tolerability and potent fungicidal activity. The greater use of Liposomal Amphotericin-B may result in an increase in the incidence of adverse effects, while Liposomal Amphotericin-B is known to have a wide margin of safety. Thus, we recommend careful monitoring and proper premedication during the treatment course with Liposomal Amphotericin-B.

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