Topical liposomal Amphotericin B (AmBisome®) as an adjunctive therapy in the management of post-traumatic invasive fungal infection (IFI).

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BACKGROUND

Topical antifungal preparations, such as Dakin's solution (sodium hypochlorite 0.4-0.5%), have been described in the management of invasive fungal infections (IFIs) in military trauma patients.[1] To our knowledge, we describe the first successful utilisation of liposomal amphotericin B (AmBisome®) to irrigate invasive infections with *Aspergillus fumigatus* and the mucoraceous mould, *Rhizopus arrhizus*, as an adjunct to aggressive surgical debridement and intravenous AmBisome® therapy.

AmBisome®

AmBisome® is a sterile, non-pyrogenic lyophilized product normally used for intravenous infusion. Amphotericin B, the active ingredient of AmBisome®, acts by binding to ergosterol on the cell membrane of susceptible fungi, inducing alterations in membrane permeability that result in fungal cell death. Liposomes are closed spherical vesicles created by mixing specific proportions of phospholipids and cholesterols so that they arrange themselves into multiple concentric bilayer membranes when hydrated in aqueous solutions.[2]

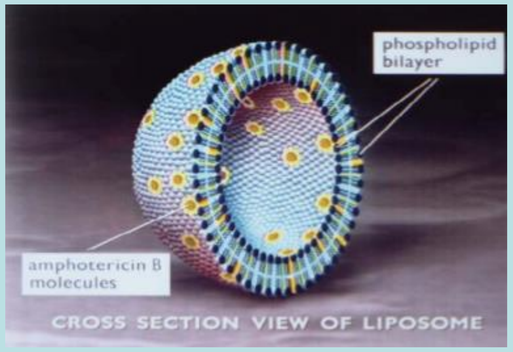

Figure 1
A schematic depiction of the liposome is presented above.[2]

CASE HISTORY

We describe the case of a 32-year-old male with type one diabetes mellitus admitted to our centre with severe polytrauma following a crush injury between a train and platform edge. The patient had a prolonged extrication and was transfused several units of packed red blood cells on scene. Initial assessment revealed complex pelvic injury with bilateral open femoral fractures, retroperitoneal haematoma, bladder rupture, perineal injury and bilateral lower limb soft tissue injuries. He required multiple debridements of his complex lower limb injuries and underwent fixation of his femoral and pelvic fractures. The right leg was deemed unsalvageable, and was amputated due to the extent of tissue loss and contamination.

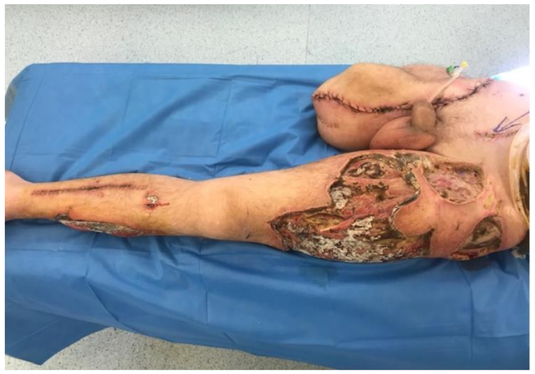

Figure 2

Figure 3

CASE HISTORY

At day 26 of admission, marked tissue necrosis and an appearance reminiscent of sub-dermal mycelial growth were noted at dressing removal on the left lower limb (Figs. 2 and 3). An infectious diseases consult was obtained, and empiric intravenous AmBisome® initiated. The patient was taken to theatre for aggressive surgical debridement of the devitalised muscle tissue (Figs. 4 and 5). In theatre, a preparation of AmBisome® 5 mg in 5% dextrose 100 ml was used to irrigate infected areas of tissue post-debridement. Tissue samples were sent for microbiology (including prolonged mycological cultures) and histology.

Figure 4

Figure 5

RESULTS

Aspergillus fumigatus and *Rhizopus arrhizus* were cultured from tissue samples at time of debridement. Serum galactomannan was negative while serum (1, 3)-β-D glucan (BDG) was raised. After aggressive surgical debridement with topical therapy and intravenous Ambisome® for 2 weeks, the patient's tissue samples from left leg were culture negative for fungi with a healthier appearance. Subsequently, the patient was able to proceed to successful skin grafting.

CONCLUSIONS

Post-traumatic IFI is a rare and devastating clinical entity with mortality rates approaching 41% in the civilian population.[3] In our patient, diabetes mellitus is a secondary risk factor for the development of IFI. While there is consensus that early, aggressive surgical debridement and systemic antifungals are vital,[1'3] the optimal therapeutic approach is unknown and there is a role for further research on adjunctive therapies to preserve tissue and reduce mortality.

It has been suggested that tissue penetration of systemic antifungals is suboptimal in IFI due to thrombosis and tissue necrosis secondary to angio-invasive mould species.[4] Thus, topical antifungal therapies may provide anti-mycotic activity at the site of disease and aid in ensuring the resolution of IFI and preventing its recurrence.

To our knowledge, this case report describes the first use of AmBisome® in liquid preparation as a topical therapy during debridement for IFI. We suggest that the direct application of a broad-spectrum, mould-active antifungal at the site of infection may assist in reducing disease burden alongside aggressive surgical management and systemic therapy. Randomised trials are necessary to determine whether such therapy adds benefit in similar patient cohorts.

REFERENCES

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