Survival in rhinocerebral mucormycosis: Is iron the key?

Sir,

I read with great interest, the study by Jayalakshmi et al., regarding factors for survival in rhinocerebral mucormycosis.[1] The mortality of patients in this series was approximately 50%, despite optimal surgical and medical management. This is similar to earlier series from across the globe. In patients with central nervous system involvement, prolonged neutropenia or disseminated disease, mortality is 80-100% despite therapy.[2] Because of its unacceptably high mortality rate, it is desirable to develop new therapeutic strategies to treat invasive mucormycosis. It is in this setting, that we must look at iron chelation, as the next possible therapeutic intervention to improve mortality and morbidity in this disorder.

Iron is required virtually by all microbial pathogens for growth and virulence. Mucorales have an exceptional iron requirement for growth and pathogenicity.[2] The potential therapeutic role of iron chelation therapy for mucormycosis was initially obscured by the paradoxically increased risk of developing mucormycosis during treatment with deferoxamine.[3] This is because, while deferoxamine is an iron chelator from the perspective of the human host, it serves as a xenosiderophore to Mucorales, which are able to strip the iron from the chelator through an energy-dependent process. However, other iron chelators do not act as iron siderophores for Mucorales. Treatment of Rhizopus-infected mice with the iron chelator deferiprone markedly improved survival. It was shown in this study that deferiprone was as effective as liposomal amphotericin B in reducing fungal burden and improving survival.[4]

In a more recent study involving the oral iron chelator deferasirox, when administered to diabetic ketoacidotic or neutropenic mice with mucormycosis, it significantly improved survival and decreased tissue fungal burden, with an efficacy similar to that of liposomal amphotericin B.[5] Most importantly, deferasirox synergistically improved survival and reduced tissue fungal burden when combined with liposomal amphotericin B.

This data from animal studies suggests the possibility of a role for iron chelation in the treatment of mucormycosis, in addition to standard anti-fungal therapy and surgery. There is a need for trials of this drug to establish usefulness in humans with this infection.

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References


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