Be vigilant in treating a patient with diabetes and COVID-19-associated mucormycosis

Dear Editor,

With all great interest, we read the recent article 'Mucormycosis and diabetes in the times of COVID-19: A Mumbai-based observational study' by Hinduja ARA *et al*.[1] By comparing survivors to nonsurvivors, the study provided insight into the epidemiology including the incidence, risk factors, site of infection, therapy and outcomes of COVID-19-associated mucormycosis (CAM) among COVID-19 patients. Mucormycosis is frequently fatal. A survey of documented mucormycosis cases discovered an overall all-cause death rate of 54%.[2,3] The fatality rate varied based on the underlying patient condition, type of fungus, and body site affected (e.g. the mortality rate was 46% among people with sinus infections, 76% for pulmonary infections, and 96% for disseminated mucormycosis).[3] We think that the study should be interpreted cautiously regarding the treatment of CAM. So, at this current juncture, we try to add some additional important points by our experience in using amphotericin B.

To reduce mortality, early treatment initiation and a multidisciplinary team approach are required. Mucormycosis is treated with a combination of surgical debridement and antifungal medication. Restricting to the guidelines of Directorate General of Health Services (DGHS), the treatment of choice is liposomal amphotericin B at an initial dose of 5 mg/kg body weight (10 mg/kg body weight in case of CNS involvement). Each vial holds 50 milligrams. It is incompatible with regular saline or ringer lactate and should be diluted in 5% or 10% dextrose. It must be continued until a favourable response is obtained and the disease is stabilized, which may take several weeks, after which it is necessary to switch to oral posaconazole (300 mg delayed release tablets twice a day for 1 day, followed by 300 mg daily) or isavuconazole (200 mg 1 tablet 3 times daily for 2 days followed by 200 mg daily). The treatment should be continued until clinical resolution of signs and symptoms of infection, resolution of radiological evidence of active disease, and removal of predisposing risk factors such as hyperglycaemia and immunosuppression, which may take a long time. If the liposomal formulation is unavailable and renal functions and serum electrolytes are within normal ranges, conventional Amphotericin B (deoxycholate) at a dose of 1-1.5 mg/kg can also be administered.[4] Amphotericin B's nephrotoxic side effects, mainly those that occur after prolonged use, are considered to be one of its major disadvantage necessitating regular monitoring of the renal function test.[5] Fever, diarrhoea, nausea, vomiting, and headache were the most common side effects associated with posaconazole therapy.[6] Isavuconazole most commonly reported side effects that include nausea, vomiting and diarrhoea. It can also cause hepatotoxicity; hence, liver enzymes should be monitored while on isavuconazole therapy.[7] Amphotericin B and posaconazole are two common antifungal drugs that cause QTc prolongation.[8] Isavuconazole can cause dose-dependent QTc interval shortening, but the clinical significance of QTc interval shortening remains unclear.[7] In our experience, we have reported more than 30 cases of adverse drug reactions of Amphotericin preparations to Pharmacovigilance Programme of India (PVPI). We know that the author is focused on mucormycosis and diabetes in CAM patients, but the data on adverse reactions will help the future researchers who are interested in this topic. Diabetes mellitus was identified as the most common underlying comorbidity for all CAM patients in the study with 73.9% of patients being known diabetics and the remaining being newly diagnosed diabetics. If so, then the diabetic diet should be established for every diabetes patient. The patient must adhere to the diet chart's timing and dosage advice. Metformin has antiviral and anti-inflammatory properties and can be given to diabetics patients with CAM.[9] Insulin doses will vary depending on the steroid type, duration and frequency of administration.[10] It would be helpful if the study addressed patients on oral hypoglycaemic medications, patients on insulin and patients who converted to insulin after therapy. Patients with random blood glucose levels exceeding 180 mg/dl should be identified and treated for diabetic ketoacidosis.[10] If a CAM patient develops diabetic ketoacidosis, we must treat them on an individual basis. Clinical data on mucormycosis treatment are limited and consequently unhelpful to clinicians. Unmet needs in mucormycosis diagnosis, treatment and education result in a poor prognosis for patients. Increasing our research and understanding of these organisms is crucial for the improvement of mucormycosis treatment.

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Conflicts of interest

There are no conflicts of interest.

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