Innovative Therapy with Caspofungin

Rajeev Soman1,
Vidyullata Koparkar2,
Anjali Shetty3, Camilla Rodrigues3

1Consultant Internal Medicine and Infectious Diseases,
2Infectious Diseases Fellow, *Consultant Microbiology,
P.D. Hinduja National Hospital and Medical Research Centre, Mumbai, Maharashtra

Dear Sir,

Candida meningitis is a rare but highly consequential disease. As per the guidelines, initial therapy is with Liposomal Amphotericin B (LAmB) with or without 5-Flucytosine.1 Step down treatment is with fluconazole. Caspofungin has poor penetration into meninges, and hence is usually not used for treating candida meningitis.

We report the successful treatment of CSF shunt associated Candida meningitis refractory to standard treatment with LAmB and 5-Flucytosine (5FC). Caspofungin was instilled intraventricularly and also used systemically in addition to the standard therapy, which resulted in cure.

A 68 year old gentleman suffered subarachnoid and intra-ventricular hemorrhage due to a basilar artery aneurysm, which was clipped. He needed multiple changes of external ventricular drain and Ommaya reservoir due to blocks. This led to nosocomial Candida albicans meningitis which was worsening despite 10 days of treatment with LAmB and 5FC to which the organism was susceptible. The susceptibilities were as follows. 5FC <1, AmB = 1, Fluconazole <1, Voriconazole <0.12, Caspofungin <0.25, Micafungin <0.06 mcg/ml.

Encouraged by our past experience of treating permanent hemodialysis catheters and chemotherapy ports with Echinocandin Lock Therapy2 and finding precedence in the literature of the use of intraventricular caspofungin in a case of Scedosporium brain abscesses in a 2 year old child3 we used caspofungin lock for the Ommaya reservoir.

We instilled at first, 5 mg caspofungin into the Ommaya reservoir to target a concentration of 2500 mcg/ml in the reservoir and planned a dwell time of 24 hours. However the patient required letting out 150 ml of CSF every 12 hours, to relieve the intra-cranial pressure. Hence we instilled 10 mg of caspofungin with a daily dwell time of 12 hours and administered the remainder of 60 mg caspofungin intravenously. This was based on a case report of refractory Candida meningitis in an immunocompromised patient cured by addition of intravenous caspofungin after failure with intravenous and intraventricular AmB and systemic fluconazole.4

We had reservations about this approach as the caspofungin preparation for intravenous use contains glacial acetic acid and has a pH of 5. Besides, we wondered whether the paradoxical effect of high concentrations of caspofungin would lead to resistance in the Candida organism.5 We could not measure caspofungin levels in the blood or CSF in order to assess the inhibitory quotient obtained in the CSF. However CSF samples obtained 3 days into treatment and several times later were found to have been rendered sterile.

The patient developed ARDS and cytopenias due to LAmB and 5FC which had to be changed to intravenous caspofungin and oral fluconazole. Treatment was continued for 20 days after which the Ommaya reservoir and VP shunt were removed and a fresh VP shunt was inserted on the contralateral side. The patient has a VP shunt and a basilar artery clip in situ, hence oral fluconazole has been continued as chronic suppressive therapy. Patient is well at follow up 1 year later.

Conclusion

In patients with candida meningitis who are refractory to usual treatment, additional intraventricular caspofungin may be an important therapeutic modality.

References