Amphotericin on the Brain

A multidisciplinary approach to improve patient outcome in refractory Candida ventriculitis

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Objective

To report a case of refractory *Candida* ventriculitis treated with intraventricular non-liposomal amphotericin B

Clinical Features

31 year old male transferred to RNSH Intensive Care Unit with several complications:

- newly diagnosed HIV
- Cytomegalovirus viraemia
- *Pneuomcystis jirovecii* pneumonia
- cervical toxoplasmosis
- *Staphylococcus aureus* infective endocarditis
- saddle pulmonary embolism
- hypoxic respiratory failure

External ventricular drain (EVD) inserted Day 4 of admission for hydrocephalus and cerebrospinal fluid (CSF) cultures taken due to ongoing fevers.

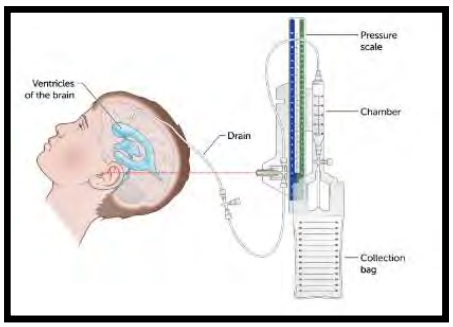

Image 1: External ventricular drain (5)

CSF cultures isolated ***Candida albicans (C.albicans)*** and patient initiated on fluconazole 400mg intravenous (IV) 12 hourly.

CSF cultures persistently positive for *C.albicans* despite 20 days of treatment.

Infectious Diseases requested pharmacy input to manufacture intraventricular non-liposomal amphotericin B deoxycholate.

Literature Review

1st line treatment for *Candida* ventriculitis is flucytosine and liposomal amphotericin B (1). Intraventricular antimicrobials are reserved for refractory ventriculitis with demonstrated success in case reports. (1-3)

Literature Review

Recommended amphotericin dose range: 0.01mg-0.5mg obtained by reconstituting powder with water for injection (WFI) and further diluted with WFI or 5% glucose (1-4)

ROYAL NORTH SHORE HOSPITAL PHARMACY DEPARTMENT
MASTER FORMULA SHEET – ASEPTIC DISPENSING

PATIENT NAME:			BATCH:				
MRN:			DATE:				
PRODUCT:	AMPHOTERICIN (FUNGIZONE) 0.25mg/mL IN WATER FOR INJECTION			PRODUCT TYPE: INTRATHECAL INJECTION			
INGREDIENTS	MASTER QTY	QTY USED	BATCH	EXPIRY	Vial size of units	T	P
AMPHOTERICIN 50mg vial (FUNGIZONE)	50mg	1vial			1 vial		
WATER FOR INJECTION BP	10mL	10mL			1 x 10mL		
AMPHOTERICIN 5mg/mL solution	5mg	1mL		(from step one)			
WATER for INJECTION	to 20mL	19mL			1 x 10mL		
CALCULATION AND PRESCRIPTION CHECKED BY:							
METHOD:							
1. Using a 10mL syringe draw up 10mL of Water for Injection B.P. and reconstitute the Amphotericin. Shake vial vigorously to dissolve. This gives a 5mg/mL solution.							
2. Using a 30mL syringe draw up 15mL of Water for Injection. Attach a syringe connector.							
3. Using a 1mL syringe, draw up 1mL of Amphotericin 5mg/mL from step (1). Add to 12. This gives a 0.5mg/mL solution. Mix contents well.							
4. Attach a brown 5 micron filter onto the other end of the dispensing connector. Prime the filter then transfer 1mL aliquots of Amphotericin 0.25mg/mL solution into a 3mL syringes. Make the 4 syringes.							
5. Expel air and cap syringes.							
CONTAINER/CLOSURE: 1mL syringe and syringe cap				NO. OF LABELS REQUIRED: 4			
EQUIPMENT REQUIRED: 1 x 20mL syringe 1 x 10mL syringe 4 x 3mL syringes 1 x brown 5 micron disc filter 2 x fluid dispensing connectors 4 x syringe caps			LABEL:				
STORAGE CONDITIONS: 2-8°C (Refrigerator)							
EXPIRY: 48hrs			LABEL CHECKED BY: FINAL CHECK:		DATE: TIME:		
MASTER FORMULA SHEET PREPARED BY:		CHECKED BY:		DATE:			

Image 2: Manufacture sheet used at RNSH to manufacture non-liposomal amphotericin for intraventricular use

Pharmacist Interventions

- Medicines Information, Antimicrobial Stewardship (AMS) and Aseptic pharmacist conducted literature review, reviewed case reports submitted by Infectious Diseases and contacted other hospital pharmacies
- Individual Patient Use endorsed by Infectious Diseases was approved by Drug Therapeutics Committee for off-label use
- In the aseptic unit, non-liposomal amphotericin was reconstituted daily with WFI and the solution filtered through a 5micron filter needle to create individual doses of 0.25mg/mL (Image 2)

Case Progress

- Neurosurgical Advanced Trainee administered 0.25mg via EVD within 30 hours of initial pharmacy referral
- Patient continued IV liposomal amphotericin 5mg/kg and flucytosine 25mg/kg every 6 hours via nasogastric tube
- Daily CSF cultures returned negative and patient demonstrated improved neurology
- Patient's surgical neck wound repeatedly cultured *C. albicans*
- Sadly, after 38 days of daily intraventricular non-liposomal amphotericin 0.25mg, the EVD blocked three times and patient was made palliative.

Discussion and Conclusion

We highlight significance of pharmacist in **a multidisciplinary approach** to optimise patient treatment, where medical literature is scarce.

Intraventricular amphotericin can be considered and safely manufactured for treatment of refractory *Candida* ventriculitis however **further research into its safety and efficacy is required.**

Acknowledgements Jessica Bui (AMS Pharmacist, RNSH) and Medicines Information (RNSH Pharmacy)

References

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