

# Management of Cryptococcal Meningitis in an Indigenous end stage renal failure patient.

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## Introduction

Cryptococcal meningitis caused by *Cryptococcus neoformans* which predominantly presents in severely immunocompromised patients. Presenting symptoms are non-specific and include headache, fever, lethargy and an altered mental state. Australian guidelines recommend 12 months of antifungal treatment in three consecutive phases in immunocompetent patients.<sup>1</sup>

## Case Presentation

The patient, an indigenous female presented to Tennant Creek Hospital with a three day history of persistent nausea, vomiting, severe neck stiffness, pain and bilateral lower limb weakness. She exhibited no obvious signs of infection and had a history of recent obstructive hydrocephalus due to an arachnoid cyst, which was surgically managed. The patient had a poor recovery post-surgery and was wheelchair bound after taking her own leave from rehab.

The patient was flown to Alice Springs Hospital (ASH) for further investigations.

Past medical history:

- » Obstructive hydrocephalus – endoscopic third ventriculostomy (Nov 2016)
- » End Stage Renal Failure (ESRF) – on haemodialysis (HD) since 2012
- » T2DM with microvascular complications
- » Hypertension
- » Severe malnutrition

## Case progress

- » The patient deteriorated quickly developing a new tremor, thought to be clonus, severe headaches that became worse after HD and was frequently hypertensive.
- » She underwent an MRI of the brain, a cerebral spinal fluid (CSF) flow study and a lumbar puncture (LP).
  - The MRI demonstrated normal CSF flow, a slight decrease in ventricle size and debris within the occipital region (consistent with Cryptococcal meningitis).
  - The LP revealed a low opening pressure, high protein (>3 g/L), low glucose (1.7 mmol/L) and was positive for Cryptococcal neoformans antigens at a titre of 1:32. Although, CSF returned nil growth of Cryptococcus.
- » They were tentatively diagnosed with Cryptococcus meningitis on the 23<sup>rd</sup> day of her admission.

## Clinical Pharmacist Involvement

- » The infectious disease team sought advice on dosing for Cryptococcus meningitis in an ESRF patient on intermittent HD, who weighs approximately 41kg.
- » As per the renal drug database;
  - Liposomal amphotericin B isn't dialysed and was dosed as per recommendations at 3mg/kg - 125mg daily and given post HD on dialysis days.
  - Flucytosine is dialysed and as such was dosed orally at 25mg/kg - 1g daily and given post HD on dialysis days.
- » As the patient was in ESRF, therapeutic concentration monitoring was recommended for flucytosine. Levels were taken prior to HD and 2 hours after the post HD dose with recommended trough and peak concentrations being >25mg/mL and <80mg/mL respectively.<sup>2</sup>

## Patient outcome

- » She was successfully treated with induction therapy (six weeks) on combination antifungals; liposomal amphotericin B and flucytosine and exhibited significant clinical improvement.
- » Four out of eight weeks of consolidation treatment, with 200mg fluconazole daily, were completed. Treatment was terminated in the setting of deranged LFTs and a consistently uncertain diagnosis.
- » Whilst admitted, she was also treated for a number of other conditions related to her co-morbidities including; pylocystitis, urosepsis, severe malnutrition, hyperglycaemia and suspected complex partial seizures
- » The patient was discharged after a 10 month hospital stay. On discharge she was able to mobilise with a 4 wheel walker and counselled on the many changes to her medications.

**Table 1**

### Cryptococcus neoformans + CSF serology

Week of admission	Week 1	Week 2	Week 3	Week 4
<b>Specimen Type</b>	CSF serum	CSF serum	CSF serum	CSF serum
<b>LPA Screen Neat</b>	POSITIVE	POSITIVE	POSITIVE	NEGATIVE
<b>Titre</b>	Reactive 1:4	Reactive 1:32	Reactive 1:16	-
<b>Protein (0.15-0.45g/L)</b>	-	>3.00	Reactive 1:17	4.83
<b>Glucose (2.7-4.2mmol/L)</b>	-	1.7	Reactive 1:18	4.1

#### References:

1. Therapeutic Guidelines, Antibiotic, July 2017 edition.
2. The Renal Drug Database, 2017.

## Conclusions:

We present a complex case of Cryptococcal Meningitis in a remote setting. Specialist knowledge from clinical pharmacists was required to aid in appropriate dosing and monitoring of antifungal therapy in this complex patient.

Whilst the patient demonstrated significant clinical improvement with antifungal therapy, this case highlights the difficulties in accurately diagnosing and treating Cryptococcal Meningitis in Central Australia.