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Inflammation and infection

Multi-route antifungal administration in the management of urinary *Candida glabrata* bezoar

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ABSTRACT

A 65-year-old lady was admitted with urosepsis and imaging suggesting right sided hydronephrosis secondary to a filling defect consistent with a fungal bezoar. An indwelling urinary catheter and a right percutaneous nephrostomy tube were inserted. Candida glabrata cultured from urine was resistant to fluconazole. Amphotericin B was instilled into the renal pelvis via the nephrostomy tube while intravenous liposomal amphotericin was administered daily along with oral flucytosine. This multi-modal antifungal administration was continued for 14 days. Clinical and biochemical improvement was achieved and repeat imaging showed complete resolution of the filling defects and hydronephrosis.

Introduction

The current management of urinary fungal infection is challenging, particularly in the management of fungal bezoars. Low-level evidence suggests surgical removal of the bezoar, combined with systemic antifungals or amphotericin B irrigation via a nephrostomy tube is effective.[1] We describe a case of a patient with a *Candida glabrata* bezoar who was managed successfully with antifungals administered via 3 different routes, including amphotericin B instillation via nephrostomy tube.

Case presentation

SP a 65-year-old woman with a background of recurrent fungal cystitis presented to a regional hospital with generalised weakness, unsteadiness and recurrent falls. She reported lower abdominal pain, blood in her urine and dysuria. Previous medical history included; poorly controlled type II diabetes mellitus and peripheral vascular disease.

On arrival to the emergency department, she was afebrile but hypotensive (blood pressure 87/61 mmHg) and in sinus tachycardia (100–120 beats/min). Her other vital signs and the remainder of her examination was unremarkable.

Investigations revealed a leucocytosis of (12 × 10^9/L) associated with a mild neutrophilia of (8.44 × 10^9/L); she was anaemic (haemoglobin 103g/L and had an acute kidney injury (AKI) with a serum creatinine of 119 micromol/L, with hyperkalaemia (6.1mmol/L) and hyponatraemia (119mmol/L). Her C-reactive protein was slightly elevated at 30mg/L. Urinalysis showed a large number of leucocytes and moderate blood; microbiology culture was initially negative. A computed tomography (CT) brain demonstrated no acute pathology. The hypotension, and AKI resolved with fluid resuscitation. An indwelling urinary catheter (IDC) was inserted but recurrent blockages occurred due to debris and clots. A repeat urine specimen grew *Candida glabrata*. She was commenced on oral fluconazole 200mg daily and transferred to a tertiary hospital for urology input.

At the tertiary hospital, a sodium chloride 0.9% bladder irrigation was commenced and a CT urogram demonstrated right hydronephrosis and an irregular filling defect extending from the right renal pelvis down to the right vesicoureteric junction, consistent with a fungal bezoar. A right percutaneous nephrostomy tube was inserted to decompress the right collecting system. *Candida glabrata* was also cultured from the right nephrostomy tube urine, resistant to fluconazole. Upon discussion with the Infectious Diseases team, amphotericin B deoxycholate (d-AMB) 25mg in 500mL glucose 5% instillation into the renal pelvis via the nephrostomy tube was commenced at a rate of 20mL/hr. Intravenous liposomal amphotericin 200mg (3mg/kg) (L-AMB) was administered daily along with oral flucytosine 1500mg (25mg/kg) 6-hourly for antifungal synergistic effect. After 4 days, the nephrostomy instillation

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Table 1
Summary of case reports of treatment of *C. glabrata* bezoar with amphotericin B deoxycholate (AMB-d) via nephrostomy tube.

Author	Patient Sex (age)	Dose and method of administration of AMB-d via nephrostomy	Concomitant systemic antifungals and duration	Duration of therapy	Outcome
Berlanga et al.[4] (2016)	F (57)	10mg/L in glucose 5% via gravity	Fluconazole, micafungin, L-AMB, AMB-d	5 days (via nephrostomy tube) 19 days (intravenous)	Full recovery after surgical removal
Rohloff et al.[5] (2017)	F (56)	50mg/500mL sterile water irrigation daily	Fluconazole, micafungin	6 days (via nephrostomy tube) 14 days (intravenous)	Full recovery without surgery

*AMB-d is incompatible with sodium chloride 0.9%.[3]

changed to L-AMB 100mg in 500mL glucose 5% at 20mL/hr due to the unavailability of d-AMB and was continued to complete 14 days. The intravenous L-AMB and oral flucytosine also continued for 14 days.

Over the course of the treatment, SP's clinical and biochemical markers of infection improved. A CT urogram at the end of the antifungal course demonstrated resolution of filling defects in the ureter. Her nephrostomy tube was removed and she was discharged with an IDC with a plan for transition to intermittent self-catheterisation to reduce subsequent urinary tract infections (UTIs). At 6 and 14-week follow up SP remains well with no features of fungal or bacterial urological infection.

Discussion

The Infectious Diseases Society of America Clinical Practice Guideline for the Management of Candidiasis suggests that management of patients with Candida UTIs associated with fungal bezoars should include surgery, systemic antifungals and d-AMB (25–50mg in 200–500mL sterile water) irrigation via nephrostomy tube.[1] *C. glabrata* isolates are frequently resistant to fluconazole and many systemic antifungals with activity against *C. glabrata* have poor penetration into the renal tract, so direct instillation of amphotericin B is also required.[1]

Published Information describing the nephrostomy tube instillation of amphotericin B is limited to case reports, with most using d-AMB. The one publication reporting L-AMB lacked dosing specifics[2] and used sodium chloride 0.9% as the administration fluid, which would be expected to cause precipitation of L-AMB.[3] Table 1 summarises the published data for d-AMB administered via nephrostomy tube for *C. glabrata* bezoar.[4,5]

There are no other reports utilising both L-AMB and d-AMB via nephrostomy tube for the treatment of fungal bezoar. Our course involved the longest duration of L-AMB via nephrostomy reported in the literature (9 days) in completing the 14 days course. Resolution of infection at 14-day review allowed cessation of therapy.

As with other cases of fungal bezoar, our patient also received systemic antifungals. We used the recommended dose of 3mg/kg daily L-AMB combined with oral flucytosine 25mg/kg 6-hourly for 14 days.[1]

Conclusion

The combination of multi-route antifungal therapy and decompression of the collecting system was successful and avoided the need for surgical source control of the *C. glabrata* bezoar in this patient. Prolonged L-AMB use via nephrostomy instillation may have contributed to clinical resolution.

Declaration of competing interest

None to declare.

Verbal and written consent was obtained from the patient in order to compile this case report.

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