Candida glabrata fungal ball cystitis is a rare complication of conservative treatment of placenta accreta: a case report

CK Wong[1*], MB, ChB, **LY Cho**[1], MB, BS, FHKAM (Obstetrics and Gynaecology), **WL Lau**[1], MB, BS, FHKAM (Obstetrics and Gynaecology), **Ingrid YY Cheung**[2], MB, ChB, FHKAM (Pathology), **Chloe HT Yu**[3], MB, BS, **IC Law**[3], MB, BS, FHKAM (Surgery), **WC Leung**[1], MD, FHKAM (Obstetrics and Gynaecology)

[1] *Department of Obstetrics and Gynaecology, Kwong Wah Hospital, Hong Kong*
[2] *Department of Pathology, Kwong Wah Hospital, Hong Kong*
[3] *Department of Surgery, Kwong Wah Hospital, Hong Kong*

* Corresponding author: wongchunkitjack@hotmail.com

Hong Kong Med J 2022;28:324–7
https://doi.org/10.12809/hkmj219449

Case report

In October 2019, a 42-year-old pregnant woman was admitted to hospital at 35+2 weeks of gestation for an elective caesarean section because of anterior placenta praevia type I and suspected placenta accreta. She was gravida 6 and parity 3+2. Her first pregnancy in 1996 resulted in a normal vaginal delivery. The second and third pregnancies were surgically terminated in the first trimester. Fourth and fifth pregnancies resulted in a lower segment caesarean section in China due to oligohydramnios and previous caesarean section.

The patient had an uneventful antenatal course in the current pregnancy. Nonetheless ultrasound examination at 35+2 weeks of gestation revealed an anterior placenta praevia type I with the placenta's leading-edge 2.7 cm from the os. A diagnosis of placenta accreta was made due to vascularities over the subserosal surface of the lower segment.

A classical caesarean section was performed after completing a course of antenatal corticosteroid at 36+4 weeks of gestation. Around four-fifths of the placenta separated spontaneously after 30 minutes. The placenta was trimmed away and 3 × 3 cm of anterior adherent placenta around the internal os was left in place. Active bleeding from the lower segment of the uterus and anterior placental bed was controlled with Sengstaken–Blakemore balloon tamponade (Rüsch Teleflex, Germany). Uterine artery embolisation was performed at the same operation by interventional radiologists. Total blood loss for the operation was 500 mL.

After surgery, the patient was transferred to the intensive care unit. Balloon tamponade was removed on day 1 (Fig 1). Prophylactic amoxicillin and clavulanate was administered intravenously after the operation. She complained of dysuria and developed a persistent swinging fever from day 2. Amoxicillin and clavulanate was switched to piperacillin/tazobactam on day 4 after blood and urine tests for sepsis. Culture of midstream urine showed *Morganella morganii* sensitive to piperacillin/tazobactam and a gram-negative bacillus. Microbiologists advised continuation of piperacillin/tazobactam for 7 to 10 days.

Examination under anaesthesia and ultrasound-guided suction evacuation were performed on day 14 due to increased per-vaginal bleeding. Intra-operatively, yellowish pus was seen leaking from the cervical os and retained product of gestation weighing 48 g was retrieved. Culture of the pus grew *Escherichia coli* sensitive to piperacillin/tazobactam. The patient again presented with fever postoperatively and blood culture revealed *E coli* septicaemia. Piperacillin/tazobactam was switched to meropenem on day 17. Blood culture sensitivity testing revealed *E coli* sensitive to meropenem and cefuroxime. Hence, meropenem was switched to cefuroxime. Ultrasound examination on day 24 revealed no evidence of retained product of gestation. Cefuroxime was continued for 14 days.

At 5-week follow-up examination, the patient reported a 1-week history of whitish debris in her urine, dysuria, and urinary frequency. Ultrasonography revealed incomplete emptying of the bladder with a lot of frothy shadows (Fig 2a). Urinary tract infection was suspected so amoxicillin and clavulanate and phenazopyridine were prescribed for 1 week. Culture of the midstream urine showed *Candida glabrata* (Fig 2b). A microbiologist was consulted and fluconazole 400 mg prescribed for 10 days.

Susceptibility testing of the *C glabrata* isolated from urine collected after admission was performed by using Sensititre YeastOne (TREK Diagnostic Systems, United Kingdom) and revealed a required fluconazole minimal inhibitory concentration of 16 μg/mL, confirming that it was in the susceptible-dose dependent category. However, the patient's symptoms persisted after completing 24 days of

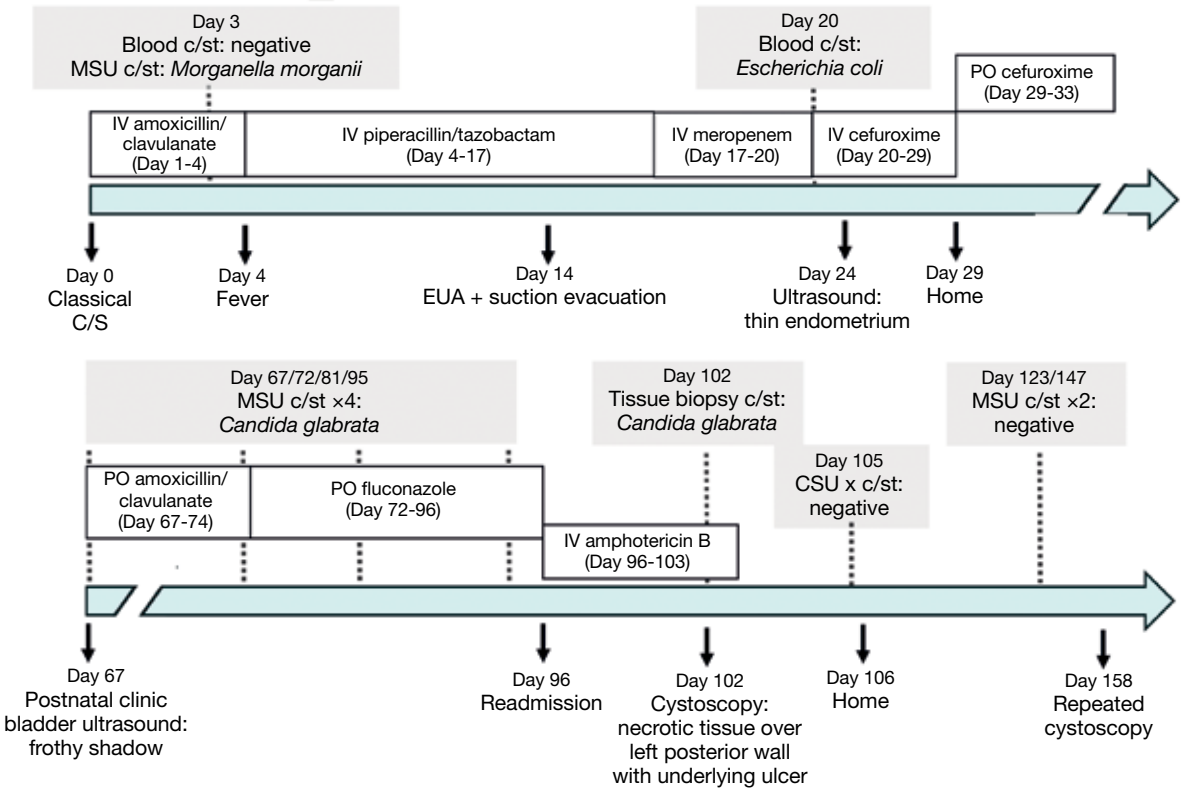

FIG 1. Timeline of patient treatment

Abbreviations: C/S = caesarean section; c/st = culture and sensitivity test; CSU = catheter specimens of urine; EUA = examination under anaesthesia; home = patient discharged home; IV = intravenous; MSU = midstream urine; PO = per oral

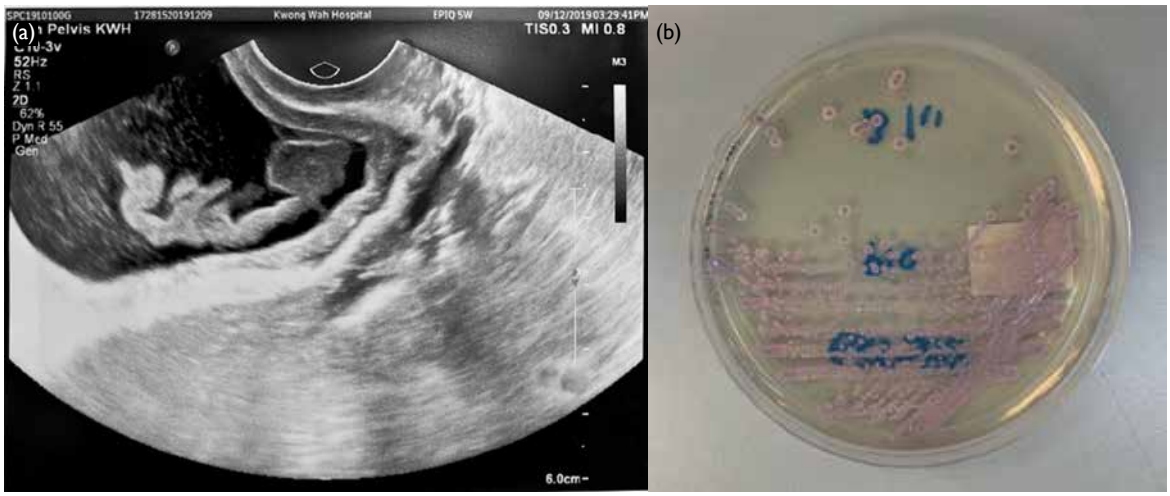

FIG 2. (a) Ultrasonograph showing "fungal debris" inside the bladder. (b) Photograph of *Candida glabrata* colony on CHROMagar Candida agar

fluconazole and ultrasound showed persistent "fungal debris" inside the bladder. She was readmitted 13 weeks after the operation for further management. Amphotericin B deoxycholate was administered intravenously for 7 days. A drug-related fever developed during the first dose but resolved after premedication with oral acetaminophen and intravenous diphenhydramine.

FIG 3. Cystoscopy images showing (a) necrotic tissue (b) and an ulcer over the bladder wall. (c) Second cystoscopy image taken 2 months later showing the healed ulcer

Flexible cystoscopy revealed necrotic tissue approximately 3 × 4 cm over the left posterior bladder wall, away from the left ureteric orifice, with an underlying ulcer (Fig 3a and b). It was removed with forceps and a basket. A fistula was suspected, and second flexible cystoscopy scheduled 2 months later. A computed tomography urogram with contrast was arranged to exclude fistula.

The second flexible cystoscopy revealed a normal bladder and a healed ulcer over the left posterior wall (Fig 3c). Computed tomography urogram showed no evidence of fistula. During postnatal follow-up, there were no urinary symptoms.

Discussion

This is the first case of *C glabrata* cystitis as a complication in our case series of planned conservative management of placenta accreta.[1] *Candida* species are a part of the normal flora of the gastrointestinal and vaginal tracts. The incidence of candiduria has been increasing in recent decades and the presence of *C glabrata* has become clinically significant due to its high resistance to routine antifungal agents. Risk factors for candiduria in our case included urinary catheterisation, intensive care unit stay, use of broad-spectrum antibiotics, female sex, and prior surgery.[2]

The placental remnants in our case induced infection and septicaemia. Subsequent prolonged use of broad-spectrum antibiotics predisposed our patient to fungal cystitis. There was no clinical or pathological evidence of placenta percreta. Chandraharan et al[3] introduced the use of the Triple-P procedure to manage patients with morbidly adherent placenta. As the Triple-P procedure removes all intrauterine placental remnants, it may reduce the risk of intrauterine infection and sepsis. Nevertheless, there is limited surgical expertise in this procedure in our unit.

Compared with other Candida species, many *C glabrata* isolates are resistant to azoles due to efflux pump–mediated resistance, genetic alterations under stress and biofilm protection.[4] A study in the United States revealed that 14% of *C glabrata* isolates were resistant to fluconazole.[5]

The presence of fungus ball/fungal bezoars in urinary tract infection is extremely rare in adults. According to treatment guidelines of the Infectious Diseases Society of America, removal of the obstructing mycelial mass by surgical or endoscopic means is strongly recommended.[6] Although culture results revealed that the *C glabrata* was susceptible-dose-dependent to fluconazole, use of fluconazole alone was likely to be insufficient due to the fungal ball in the bladder. A multidisciplinary approach including microbiologists and urologists is essential.

In symptomatic Candida cystitis, first-line treatment is oral fluconazole 200 mg daily for 2 weeks. For fluconazole-resistant *C glabrata*, amphotericin B deoxycholate or oral flucytosine are the drugs of choice. Around 50% of patients prescribed an amphotericin B infusion experience infusion-related adverse events, such as fever, chills, rigors, hypotension, and rarely, hypokalaemia resulting in ventricular fibrillation. In addition, renal toxicity is a well-known adverse effect.[5] Close monitoring of renal function and electrolytes is essential.

Placenta accreta spectrum treated conservatively by leaving the placenta in situ is a recognised and successful management option, but is associated with risks of infection or postpartum haemorrhage. Our case demonstrates

that fungal infection can develop during the period of conservative management and requires multidisciplinary consultation.

Author contributions

Concept or design: CK Wong, WC Leung.
Acquisition of data: All authors.
Analysis or interpretation of data: All authors.
Drafting of the manuscript: CK Wong, WC Leung.
Critical revision of the manuscript for important intellectual content: All authors.

Conflicts of interest

The authors have no conflicts of interest to disclose.

Acknowledgement

The authors thank interventional radiologists Dr KH Lee and Dr CW Tang for their contributions to this report.

Funding/support

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethics approval

The patient was treated in accordance with the Declaration of Helsinki, provided informed consent for all treatments and procedures, and provided consent for publication.

References

1. Lo TK, Yung WK, Lau WL, Law B, Lau S, Leung WC. Planned conservative management of placenta accreta—experience of a regional general hospital. J Maternal Fetal Neonatal Med 2013;27:291-6.
2. Gajdács M, Dóczi I, Ábrók M, Lázár A, Burián K. Epidemiology of candiduria and Candida urinary tract infections in inpatients and outpatients: results from a 10-year retrospective survey. Cent European J Urol 2019;72:209-14.
3. Chandraharan E, Rao S, Belli A, Arulkumaran S. The Triple-P procedure as a conservative surgical alternative to peripartum hysterectomy for placenta percreta. Int J Gynecol Obstet 2012;117:191-4.
4. Rodrigues CF, Silva S, Henriques M. *Candida glabrata*: a review of its features and resistance. Eur J Clin Microbiol Infect Dis 2013;33:673-88.
5. Pfaller MA, Messer SA, Hollis RJ, et al. Variation in susceptibility of bloodstream isolates of *Candida glabrata* to fluconazole according to patient age and geographic location in the United States in 2001 to 2007. J Clin Microbiol 2009;47:3185-90.
6. Pappas PG, Kauffman CA, Andes DR, et al. Executive Summary: Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. Clin Infect Dis 2016;62:409-17.