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CASE REPORT

Colovesicular fistula from *Candida dubliniensis* in an immunocompetent resulting in poor outcome

Christine Rizkalla, Jillian Ottombrino and Fahad Malik

ABSTRACT

Candida dubliniensis is a rare fungal opportunistic infection originally isolated from the oral cavity of severely immunocompromised individuals. We present a case of a candidiasis infection in a patient with only decompensated liver cirrhosis and diabetes mellitus as his immunocompromising risk factors, resulting in severe fungemia and death within 5 days despite being on antifungal therapy.

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KEYWORDS
Candida dubliniensis; cirrhosis; fungemia; colovesicular fistula

1. Introduction

Candida albicans is historically known to be the most prevalent and pathogenic of the species however, new evidence shows a decline in the incidence of *C. albicans* infection, with a shift towards the emergence of *Candida dubliniensis*. *C. dubliniensis* is distributed worldwide and is primarily pathogenic in diseases of the oral cavity [2]. *Candida dubliniensis* was first described as a novel species in 1995 [3]. It is a chlamydospore and germ tube positive yeast which has recently been primarily exhibited in the oral cavities of HIV/AIDS patients.

Recent research is beginning to identify *C. dubliniensis* as a minor organism that is primarily within the oral microflora, as well as being independently pathogenic in disease processes. This yeast is rarely found in oral cavities of healthy individuals and unlikely to result in bloodstream infections. The current prevalence of *C. dubliniensis* is 1.2% but is becoming more common as a source of infection in immunocompromised patients [5]. We report the first possible case of *Candida dubliniensis* in a patient with decompensated liver disease and diabetes mellitusas his two immunocompromising risk factors, resulting in severe fungemia and colovesicular fistula resulting in his death within 5 days, while on antifungal therapy. His diabetes mellitus type 2 was well controlled as his HbA1 C was 6.2%.

2. Case history

A 55 year-old male with a past medical history of hypertension, diabetes mellitus, liver cirrhosis due to Hepatitis C (treated with ribavirin and sustained virological response status achieved) and alcohol abuse, brought in by ambulance to the emergency department after he was found to be lethargic, lying on the floor at home.

On physical examination, he was a middle-aged male and appeared his age. He was afebrile but hypotensive with blood pressure of 74/50 and bradycardic with a pulse rate of 49. He was awake, alert and able to verbalize but severely confused. He had yellow discoloration of his skin along with scleral icterus. The abdomen was soft, nontender, and mildly distended. Extremities showed +3 pitting edema.

White Blood Cells 5.1 k/ul, hemoglobin 6.4 g/dl, platelets 262 k/ul, sodium 136 mmol/L, potassium 6.1 mmol/L, BUN 85 mg/dL, creatine 5.9 mg/dL, Anion Gap 24.1 mmol/L, estimated GFR (MDRD) 10.00 mL/min, lactic acid level 4.5 mmol/L, total bilirubin 6.2 mg/dL, Aspartate Aminotransferase (AST/SGOT) 252 U/L, Alanine Aminotransferase (ALT/SGPT) 117 U/L, Alkaline Phosphatase 560 U/L, Ammonia <10umol/L, troponin I 0.064 ng/ml, total protein 6.4 g/dL, albumin 2.6 g/dL, PT 22.9 SEC, APTT 37 SEC, PT-INR 2.02. Initially, the first two collected samples of blood cultures showed no growth. Urinalysis was positive for red and white blood cells along with proteins and leukocyte esterase. Clean catch urine culture revealed 50,000–99,000 CFU/mL of yeast isolated. All labs were within normal ranges one-year prior.

Electrocardiogram showed sinus bradycardia of 49 with fusion complexes, low voltage QRS, Chest x-ray was normal. Ultrasound of abdomen revealed hepatomegaly with liver cirrhosis, splenomegaly of 14 cm, and a small amount of ascites. Abdominal paracentesis showed no evidence of infection.

He was managed in the intensive care unit for treatment of hepatorenal syndrome with hemodialysis, blood transfusion, intravenous fluids, midodrine, low dose norepinephrine (2–6 mcg), 100 mg hydrocortisone, pantoprazole, antibiotic (meropenem), octreotide and lactulose. He continued to be afebrile with no evidence of leukocytosis, but mental status

CONTACT Christine Rizkalla chrisrizkalla@gmail.com

continued to deteriorate. He had worsening of his synthetic liver functions with INR, up to 4.09. During the course of his admission, he also had a sudden drop in hemoglobin from 8.6 to 6.4 with inability to protect his airway requiring tracheal intubation with mechanical ventilation. A triple lumen catheter was also placed at the time and he underwent an urgent upper endoscopy for suspicion of variceal bleeding. The endoscopy revealed medium-sized varices and portal hypertensive gastropathy but no active bleeding at the time. A large amount of old blood was found in the gastric fundus.

Eventually, 2 weeks later, he showed significant clinical improvement in mental status and achieved hemodynamic stability. He was liberated from mechanical ventilation, tapered off from norepinephrine and downgraded to a general medical floor. While on the floor, he again became confused and complained of dysphasia with white blood cells elevated to 17,000 k/ul. Two repeat blood cultures from different sites grew *Candida dubliniensis*. All central venous catheters and lines were removed but did not show any growth. A repeat paracentesis was again negative for any infections and cultures had no growth. At this time, the urine had foul odor and showed fecal-matter-like discoloration. The microscopy of the UA revealed large amounts of yeast growth as well. This was attributed to a possible colovesicular fistula. He was started on micafungin but quickly became unstable for any surgical intervention and he expired 5 days later.

3. Discussion

C. dubliniensis has morphological and biological characteristics that are very similar to *C. albicans*, urging for the need of speciation of the two species due to *C. dubliniensis* resistance of fluconazole [6,7]. This yeast should not be dismissed as a colonization due to lack of studies on it. *C. dubliniensis* has a prevalence of 1.2% but is becoming more common as a source of infection [5]. This yeast infection has shown to be increasing in incidence with infections outside of the oral cavity, mainly bloodstream infections. This is likely due to growing resistance to fluconazole [5,8]. In studies, *C. dubliniensis* showed limited ability to cause invasive infection due to lack of hyphal transformation and virulence genes [9,10].

There is high mortality of up to 30% related to Candidial infections [4,11]. There have been cases found to have invasive candidiasis resulting in poor outcomes or death discovered on autopsy [12,13]. In our patient, the most considerable cause of his expiration was fungemia due to colovesicular fistula likely resulting in septic shock along with his comorbidities. The Candida species is not commonly known to create colovesicular fistulas especially in such a short amount of time and without any prior surgical history. Therefore, fungal infections should always be considered in these types of cases [14,15].

4. Conclusion

This case raises awareness of invasive infection from *C.dubliniensis* which could result in life-threatening infections, even with lack of hyphae. Fungal hyphae extend by tip growth in a process that encompasses the polarized transport of vesicles to growth sites, where they fuse to ensure the localized deposition of new plasma membrane and cell wall material, thus making hyphae a tool for pathogenicity for the organism [16]. Early diagnosis and aggressive antifungal treatment could change the outcome but as more research is needed on this topic to understand the pathogenicity. Micafungin was chosen as our antifungal of choice as it is specific to the Candida species.

Disclosure statement

The authors declare that there are no conflicts of interest regarding the publication of this paper.

ORCID

Christine Rizkalla http://orcid.org/0000-0002-6359-5334
Jillian Ottombrino http://orcid.org/0000-0002-3728-0400
Fahad Malik http://orcid.org/0000-0002-0956-5708

References

[1] Moran GP, Coleman DC, Sullivan DJ, et al. *Candida albicans* versus *Candida dubliniensis*: why is C. albicans more pathogenic? Int J Microbiol. 2012;2012:205921.
[2] Sullivan D, Coleman D. *Candida dubliniensis*: characteristics and identification. *J Clin Microbiol* Am Soc Microbiol J. 1998 Feb 1;36(2):329–334. .
[3] Derek J. Sullivan, Gary P. Moran, David C. Coleman, Candida dubliniensis: Ten years on, FEMS Microbiology Letters, Volume 253, Issue 1, December 2005, Pages 9–17, https://doi.org/10.1016/j.femsle.2005.09.015
[4] Morgan J, Meltzer MI, Plikaytis BD, et al. Excess mortality, hospital stay, and cost due to candidemia: a case-control study using data from population-based candidemia surveillance. Infect Control Hosp Epidemiol. 2005;26:540–547.
[5] Khan Z, Ahmad S, Joseph L, et al. *Candida dubliniensis*: an appraisal of its clinical significance as a bloodstream pathogen. PloS One. 2012;7(3):e32952.
[6] Benedetti VP, Savi DC, Aluizio R, et al. Analysis of the genetic diversity of Candida isolates obtained from diabetic patients and kidney transplant recipients. Mem Inst Oswaldo Cruz. 2016;(7).
[7] Colombo AL, Guimarães T, Camargo LF, et al. Brazilian guidelines for the management of

candidiasis: a joint meeting report of three medical societies: sociedade Brasileira de Infectologia, SociedadePaulista de Infectologia, SociedadeBrasileira de Medicina Tropical. Braz J InfectDis.[online]. 2013; 17(3):283–312. https://doi.org/10.1016/j.bjid.2013.02.001..

[8] Moran GP, Sullivan DJ, Henman MC, et al. Antifungal drug susceptibility of oral *Candida dubliniensis* isolates from HIV-infected and non-HIV-infected subjects and generation of stable fluconazole-resistant derivatives in vitro. Antimicrob Agents Chemother. 1997;41:617–623.

[9] Moran GP, Coleman DC, Sullivan DJ. *Candida albicans* versus *Candida dubliniensis*: why is *C. albicans* more pathogenic? Int J Microbiol. 2011. Epub 2011 Sep 4. DOI:10.115/2012/:205921

[10] Stokes C, Moran GP, Spiering MJ, et al. Lower filamentation rates of *Candida dubliniensis* contribute to its lower virulence in comparison with *Candida albicans*. Fungal Genet Biol. 2007;44:920–931.

[11] Phua AI-H, Hon KY, Holt A, et al. Candida catheter-related bloodstream infection in patients on home parenteral nutrition - Rates, risk factors, outcomes, and management. Clin Nutr ESPEN. 2019;31:1–9.

[12] Aghdam M, Reza F, Sund S. Invasive esophageal candidiasis with chronic mediastinal abscess and fatal pneumomediastinum. Am J Case Rep. 2016 Jul 8;17: 466–471. .

[13] Piubelli MLM, Felipe-Silva A, Kanegae MY, et al. Fatal necrotizing *Candida* esophagitis in a patient with leukocytoclastic cutaneous vasculitis and ankylosing spondylitis. Autops Case Rep. 2019 Mar 22;9(2): e2018070. .

[14] Al-Shawwa B, D'Andrea L, Quintero D, et al. Candida esophageal perforation and esophagopleural fistula: a case report. J Med Case Rep. 2008 Jun 17;2(1):209. .

[15] LEFKOWITZ M, ELSAS LJ, LEVINE RJ. Candida infection complicating peptic esophageal ulcer: infection in an aortic-esophageal fistula. Arch Intern Med. 1964;113(5):672–675.

[16] Riquelme M, Aguirre J, Bartnicki-García S, et al. Fungal morphogenesis, from the polarized growth of hyphae to complex reproduction and infection structures. Microbiol Mol Biol Rev. 2018;82(2): e00068–17.