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

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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.

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 mellitusus 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 HbA1C 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 bradycardiac 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...
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.

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