CASE REPORT

Persistent spontaneous fungal peritonitis secondary to *Candida albicans* in a patient with alcoholic cirrhosis and review of the literature

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SUMMARY

Candida albicans is a common human pathogen. Occasionally, it can cause peritonitis in immunocompromised and postsurgical patients. We report a case of a male patient who presented with abdominal pain and distention. He had a history of end-stage liver disease secondary to alcoholism. His peritoneal fluid culture revealed *C. albicans*, and (1–3)- β -D glucan (BDG) level was elevated. His hospital course was complicated by sepsis and renal failure. He was treated with antifungals for spontaneous fungal peritonitis. Fungal peritonitis should be suspected in patients with chronic liver disease particularly with elevated BDG levels.

BACKGROUND

Candida albicans constitutes a part of normal oral, gastrointestinal and vaginal flora, and it can transform into a pathogen in immunocompromised patients.¹ Disseminated infection can present with oral thrush, esophagitis and infective endocarditis. Very rarely, *C. albicans* can cause spontaneous fungal peritonitis (SFP) in patients with chronic liver disease.² SFP has clinical presentation similar to spontaneous bacterial peritonitis (SBP) with symptoms of abdominal pain, distention and fever. Diagnosis can either be made by peritoneal fluid culture, serological testing or by elevated serum (1–3)- β -D glucan (BDG). Treatment involves the use of antifungal agents like fluconazole or an echinocandin. The purpose of this report is to highlight the association between *C. albicans* and SFP in patients with cirrhosis, and how this devastating condition can be addressed promptly to avoid adverse outcomes.

CASE PRESENTATION

A 56-year-old White man with medical history of end-stage liver disease secondary to chronic alcoholism presented with abdominal pain, distention, nausea and vomiting lasting for 5 days. He denied any haematemesis, melena, diarrhoea, altered level of consciousness, fever, chills, night sweats or urinary abnormalities. On presentation, he had a temperature of 36.6°C, a respiratory rate of 18 bpm and a blood pressure of 123/59 mm Hg. Abdominal examination revealed caput medusa with purpura on bilateral lower quadrants, diffuse abdominal tenderness, abdominal distension and positive shifting dullness suggestive of ascites. Liver and spleen were non-palpable due to significant

ascites. Rest of the physical examination was unremarkable.

INVESTIGATIONS

Laboratory investigations revealed haemoglobin level 15.6 g/dL, white cell count 2190 cells/ μ L, platelet count 137 000/ μ L, blood urea nitrogen 6 mg/dL, serum creatinine level 0.85 mg/dL, aspartate transaminase 20 IU/L, alanine transaminase 25 IU/L, alkaline phosphatase 109 IU/L, total bilirubin 1.4 mg/dL, lactic acid 2.4 mmol/L, amylase 150 IU/L and albumin 3.4 g/dL. His MELD score was 27.

Blood cultures on admission turned positive for *Klebsiella oxytoca*. Diagnostic paracentesis was performed initially and showed no evidence of SBP. The patient underwent repeated paracentesis, and peritoneal fluid cultures grew *C. albicans* on cornmeal agar plates (figure 1). Gram staining also revealed pseudohyphae arising from yeast cells (figure 2). Serum BDG level was 305 pg/mL (normal 61 pg/mL). MRI abdomen/pelvis on admission showed some fluid collection around pancreas and changes of chronic pancreatitis with dilation of pancreatic duct (figure 3). Postcontrast MRI showed severe peritoneal and omental thickening consistent with peritonitis (figure 4).

DIFFERENTIAL DIAGNOSIS

On presentation, the differentials were spontaneous bacterial/fungal peritonitis, pancreatitis and

Figure 1 Corn meal agar plate showing growth of *Candida albicans* with pseudohyphae.

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Figure 2 Pseudohyphae seen arising from oval shaped, yeast cells usually stain Gram-positive.

Figure 3 MRI axial fat-saturated T2-weighted image showing septations consistent with lobulated peritoneal fluid collections.

cholecystitis. However, laboratory and imaging studies ruled out these possibilities.

TREATMENT

The patient was hospitalised and initiated on intravenous antibiotics (metronidazole and levofloxacin). He developed acute kidney injury which was thought to be secondary to hepatorenal syndrome for which he required intermittent haemodialysis.

On third day of hospitalisation, the patient became altered, drowsy with worsening abdominal pain. He became hypotensive 90/60 mm Hg, tachycardic (120 bpm) and febrile. Antibiotics were switched to intravenous meropenem when blood cultures on admission turned positive for *K oxytoca*.

Intravenous micafungin was added after *C albicans* grew on ascitic cultures. The patient continued to have *C albicans* growing on repeated ascitic fluid cultures, and he also grew *C albicans* from urine cultures. Intravenous fluconazole was added due to persistent positive peritoneal fluid cultures and candiduria. Intravenous meropenem was stopped after finishing a 2-week course for *Klebsiella* bacteraemia. Fluconazole was switched to oral, and intravenous micafungin was continued.

OUTCOME AND FOLLOW-UP

The patient was discharged on intravenous micafungin and oral fluconazole, with a plan to treat for 4 weeks. His ascitic cultures

Figure 4 MRI axial postcontrast T2 image showing peritoneal thickening and enhancement consistent with peritonitis.

became negative after 3 weeks. Serum BDG levels decreased from 305 pg/mL to 210 pg/mL. However, he later decided to stop treatment as he went to home hospice given his severely malnourished status.

DISCUSSION

Spontaneous peritonitis is a common condition. It is usually seen in patients with end-stage liver disease and ascites. The most common underlying cause for spontaneous peritonitis is bacterial infection; however, very rarely fungal infections can be the causative agents.^{2 3} Most reported cases of *Candida* peritonitis are secondary (after surgery or gut perforation).⁴ Available literature on SFP is scarce, only few case reports and a couple of case series of spontaneous peritonitis due to *C. albicans* have been reported so far in patients with chronic liver disease.^{2 5-9} We are reporting a case of SFP presenting in a unique fashion that persisted for 3 weeks until the patient was treated with dual therapy (micafungin and fluconazole).

SFP mostly presents with abdominal pain, distension and guarding. Patients can have associated symptoms of fever, paralytic ileus and tachycardia. Since SFP is clinically indistinguishable from SBI, patients are usually treated with empiric antibiotic therapy. In one study, 92% of patients with SFP had prior exposure to antibiotics in the last 1-month.¹⁰

Fungal cultures of the ascitic fluid are considered to be the gold standard for the diagnosis of SFP. However, it is difficult to distinguish true pathogens from contaminants.¹⁰⁻¹² Furthermore, fungal cultures can appear negative due to prophylactic antifungal therapy or difficulty to culture due to other unknown reasons.¹² Since conventional microbiological procedures have diagnostic limitation, ascitic fluid BDG levels have recently been used.^{11 13} Serum antibody detection test against *C albicans* germ tube antibodies (CAGTA) and PCR have also been proposed.¹⁴ All of these diagnostic modalities are quicker than cultures and can identify more patients with candidiasis.¹⁵

BDG is a component of fungal cell wall, and its presence in the serum or ascitic fluid signifies fungal infection. Low BDG levels potentially rule out the disease as it has a high sensitivity.¹⁶ Elevated serum BDG levels are indicative of fungaemia in patients with malignancies or those in intensive care units.¹⁷ Similarly, monitoring levels of BDG can be used to assess treatment response.¹⁸ At cut-off of 240 pg/mL, the sensitivity and specificity of the assay are 100% and 83%, respectively, for the diagnosis of invasive fungal infections.¹⁹ However, BDG levels when combined with clinical and microbiological findings can

be a good screening tool because of the high sensitivity and specificity.²⁰ In our case, the reduction of serum BDG levels along with symptomatic recovery with antifungal therapy and repeat negative peritoneal culture after treatment excluded the possibility of false-positive results and also proposed the diagnostic utility of serum BDG for SBP.

Serum CAGTA can also be used for the diagnosis of fungal peritonitis.¹⁴ One study showed that CAGTA has a sensitivity and specificity above 85% and can be detected in serum earlier than tissue culture became positive.²¹ Furthermore, CAGTA titres complement blood cultures in invasive candidiasis, not only for diagnosis but also for therapeutic monitoring.^{21–22} Other testing modality includes polymerase chain reaction (PCR) for detection of fungal DNA; it has been regarded as a quicker technique with very reliable results but more studies are needed to determine its efficacy for the diagnosis of SFP.²³

The Infectious Disease Society of America suggests echinocandin as the initial drug of choice for intra-abdominal infections in patients with isolates that are resistant to azoles, and for critically ill patients with poor response to azoles.^{15–24} Moreover, high-risk patients (immunocompromised, prolonged hospital stay, prior antibiotic therapy) and those who had previously been treated with azoles should be treated with an echinocandin.²⁵ Fluconazole can be used as an acceptable alternative to echinocandin in selected cases, including patients with low-risk features and no prior azole exposure.^{15–26} One retrospective study of patients with community-acquired candidemia in three tertiary care hospitals showed that all isolates of *C. albicans* and 85% of *Candida* spp were susceptible to voriconazole and fluconazole.²⁷ Another study of 31 patients also showed that the majority of patients with *Candida* spp were susceptible to fluconazole therapy.²⁸ Furthermore, fluconazole has good oral and parenteral bioavailability, excellent peritoneal penetration and also has a good side-effect profile (in non-cirrhotic patients).²⁴ In our case, initial poor response to micafungin and candiduria prompted us to add intravenous fluconazole as a dual therapy.

Peritoneal lavage can also be used in combination with antifungals to treat refractory infections. It is also important to remove all invasive catheters and implantable ports such as intravenous catheters, peripherally inserted central catheter, Foley catheter and address the underlying predisposing condition. In cases of peritoneal abscess, surgical or radiological drainage is necessary.²⁹

Fungal peritonitis has a very poor prognosis in patients with cirrhosis.⁴ In one study, all patients with symptomatic SFP who were

not treated with antifungals died by the end of 1-year of follow-up, compared to around 50% of the asymptomatic patients with positive culture for *Candida* spp who did not get therapy.³⁰ One systematic review of 2761 randomised patients in 11 large-scale clinical trials showed that untargeted prophylactic antifungal therapy can effectively decrease the risk of dissemination but more studies are needed to establish its mortality benefits.³¹

Contributors AM and WU wrote the discussion and did literature review. UZ and MAIM wrote case presentation and summary. All authors were involved in patient care.

Competing interests None declared.

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Learning points

- Physicians should have a high suspicion for spontaneous fungal peritonitis especially in high-risk patients and when the initial response to antibiotics is poor.
- Diagnostic techniques such as fungal cultures and serum (1→3)-β-D glucan should be adopted particularly in patients with cirrhosis and end stage renal disease.
- Physicians should have a low threshold for starting empiric prophylactic antifungal therapy in high-risk patients especially when symptoms persist despite antibiotics therapy to avoid high mortality.
- Larger-scale studies are needed to determine benefits of pre-emptive antifungal therapy and to devise diagnostic criteria and therapeutic protocols for SFP.

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