Case report

Peritonitis caused by *Blastomyces dermatitidis* in a kidney transplant recipient: case report and literature review

J.A. Barocas, G.M. Gauthier. Peritonitis caused by *Blastomyces dermatitidis* in a kidney transplant recipient: case report and literature review. Transpl Infect Dis 2014. All rights reserved

**Abstract:** *Blastomyces dermatitidis* is a dimorphic fungus endemic to the midwestern, south-central, and southeastern United States known to cause disseminated infection in immunocompromised individuals. We report a case of *B. dermatitidis* peritonitis in a renal allograft recipient with new-onset ascites and cytomegalovirus encephalitis. Peritoneal blastomycosis is a rare clinical entity and, to our knowledge, this patient represents the first known case of peritoneal blastomycosis in a solid organ transplant recipient. We review the clinical characteristics of *B. dermatitidis* peritonitis as well as the literature on fungal peritonitis with emphasis on dimorphic fungal pathogens. Clinical features suggestive of fungal peritonitis include new-onset ascites, abdominal pain, and fevers, especially with antecedent or concomitant pneumonia. A high index of clinical suspicion, along with the use of culture and non-culture diagnostics, is needed for early diagnosis and prompt initiation of therapy.

*Blastomyces dermatitidis*, the etiologic agent of blastomycosis, is a dimorphic fungus that is endemic to the midwestern, south-central, and southeastern areas of the United States and several provinces in Canada. In the soil, *B. dermatitidis* grows as a filamentous mold that produces infectious conidia. Conidia or mycelial fragments enter the lungs via inhalation and convert into pathogenic yeast. The clinical spectrum of disease is varied, and includes asymptomatic infection, acute or chronic pneumonia, and disseminated disease. Persons with intact and impaired immunity are at risk for blastomycosis following environmental exposure. Once infection is established in the lungs, *B. dermatitidis* frequently disseminates to the skin and bone. Dissemination to other tissues, such as the peritoneum, is uncommon and can be clinically challenging to diagnose. We report a case of *B. dermatitidis* infection of the peritoneal fluid in a solid organ transplant (SOT) recipient with new-onset ascites. In addition, we review the literature on fungal peritonitis with emphasis on dimorphic fungal pathogens.

**Case report**

A 68-year-old man on intravenous ganciclovir for treatment of cytomegalovirus (CMV) encephalitis was readmitted to the hospital for evaluation of worsening confusion, abdominal pain, and fever (38.1°C). He was immunocompromised after a living unrelated-donor renal transplant performed 1 year earlier for end-stage renal disease (ESRD) caused by hypertension. Pharmacologic immunosuppression consisted of basiliximab induction followed by prednisone, mycophenolate mofetil, and tacrolimus. He had previously been hospitalized 48 days earlier for CMV encephalitis and laparoscopic drainage of a perinephric lymphocele (cultures were not obtained).
Physical exam at readmission demonstrated a mildly firm and distended abdomen without appreciable fluid wave, and diminished breath sounds in the lung bases. Pertinent admission labs included white blood cell count 1.9 K/μL (3.8–10.5 K/μL), creatinine 0.84 mg/dL (0.70–1.20 mg/dL), C-reactive protein 23 mg/dL (0–1 mg/dL), and erythrocyte sedimentation rate 107 mm/h (0–15 mm/h).

Diagnostic evaluation included blood cultures, transesophageal echocardiogram, chest x-ray, and computed tomography (CT) of the abdomen-pelvis. Blood cultures obtained from peripheral sites grew vancomycin-resistant *Enterococcus faecium*. The transesophageal echocardiogram was negative for valvular vegetations. Chest x-ray showed new opacifications in the medial aspect of both lower lobes with air bronchograms. Daptomycin and levofloxacin were started to treat a catheter-related bloodstream infection and presumed bacterial pneumonia, respectively. The abdominal-pelvic CT scan demonstrated recurrence of the perinephric fluid collection (5.3 × 6.0 × 5.2 cm).

Cultures from a percutaneously placed perinephric drain grew vancomycin-resistant *E. faecium*; fungal cultures were not obtained.

On hospital day 5, he developed worsening confusion, hypotension, new-onset ascites, and hypercarbic respiratory failure requiring mechanical ventilation. He was continued on daptomycin and his anti-infectives were broadened to include tigecycline and cefepime for empiric treatment of hospital-acquired pneumonia as well as intra-abdominal abscess. A repeat CT scan of his chest, abdomen, and pelvis demonstrated bilateral pulmonary nodules, a large amount of ascites, and a decrease in the size of his percutaneously drained perinephric fluid collection (Fig. 1). A paracentesis and bronchoscopy were performed. The peritoneal fluid had 115/μL nucleated cells (61% neutrophils, 17% lymphocytes, and 0% eosinophils). The serum-ascites albumin gradient was 0.4. Calcofluor staining of bronchoalveolar lavage and ascitic fluid specimens demonstrated broad-based budding yeast on smear and cultures grew *B. dermatitidis*. Blastomyces urinary antigen was above the level of quantitation (>14.7 ng/mL). He was started on liposomal amphotericin B 5 mg/kg/day on hospital day 6.

Despite aggressive antifungal therapy, he remained hypotensive, acidotic, and was unable to wean from the ventilator. A family meeting was held, aggressive life-prolonging measures were discontinued, and comfort care measures were initiated. The patient died on hospital day 15. Autopsy was not performed. His only known risk factor for blastomycosis was residence in an endemic area.

**Discussion**

Blastomycosis is an uncommon infection in SOT recipients with an incidence of 0.13–0.14% (1, 2). The lungs are the most common site of infection and disseminated disease occurs in 36–50% (1, 2). The skin is the most frequent site for dissemination (1, 2). *B. dermatitidis* infection of other organs (e.g., central nervous system) is uncommon in transplant recipients (1) and, to our knowledge, the patient described here is the first known case of peritoneal blastomycosis in a patient immunosuppressed after solid organ transplantation. In addition to disseminated disease, SOT recipients are at high risk for respiratory failure including acute respiratory distress syndrome from *B. dermatitidis* (1, 3). Suppression of innate and adaptive immunity by anti-rejection medications, such as mycophenolate and tacrolimus, may predispose patients to developing complicated or severe blastomycosis. The use of monoclonal antibodies, such
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<td>1</td>
<td>M</td>
<td>68</td>
<td>Confusion, abdominal pain, fever (38.1°C)</td>
<td>Renal transplant</td>
<td>Chest–abdomen–pelvic CT; Bilateral pulmonary nodules; new-onset ascites</td>
<td>Lungs</td>
<td>115/µL nucleated cells (61% neutrophils, 17% lymphocytes, and 0% eosinophils)</td>
<td>Culture of ascitic fluid grew <em>Blastomyces dermatitidis</em>; Positive <em>Blastomyces</em> urinary antigen</td>
<td>Lipid amphotericin B</td>
<td>Died</td>
<td>Barocas &amp; Gauthier (PR)</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>28</td>
<td>Increasing abdominal girth, dyspnea, fever (38.1°C)</td>
<td>No CT chest; Nodular pleural thickening</td>
<td>Fallopian tubes, ovaries</td>
<td>4 WBC/mm³</td>
<td>Tubo-ovarian abscess (TOA), pyogranulomas in the fallopian tubes, peritoneal nodules with <em>B. dermatitidis</em>; Fungal cultures of TOA and peritoneal nodules grew <em>B. dermatitidis</em></td>
<td>Surgical debridement and right salpino-oophorectomy, Itraconazole × 6 months</td>
<td>Survived</td>
<td>Mouzin &amp; Beilke (14)</td>
<td></td>
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<td>3</td>
<td>M</td>
<td>54</td>
<td>LUQ pain, fevers, chills, left knee pain, 5 kg weight loss for duration of 1 month</td>
<td>No CXR; Small pleural effusion; ultrasound: 4 × 6 cm multiloculated splenic abscess</td>
<td>Omentum</td>
<td>2 L of ascitic fluid drained, no studies performed</td>
<td>Nodules of peritoneum and omentum showed caseating granulomas, broad-based budding yeast, and cultures grew <em>B. dermatitidis</em></td>
<td>Diagnostic laparotomy, ketoconazole × 5-6 months</td>
<td>Survived</td>
<td>MacDonald et al. (8)</td>
<td></td>
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<tr>
<td>4</td>
<td>M</td>
<td>37</td>
<td>Three months of increasing abdominal girth, RUQ pain, early satiety, nausea, vomiting, melanic stools, weight loss, fevers, and night sweats</td>
<td>No CXR; No pulmonary disease; abdominopelvic CT: ascites</td>
<td>Serosal surface small bowel and diaphragm</td>
<td>pH 7.4, protein 5.3 g/dL, LDH 88, Amylase 55, Glucose 88, RBC 276, WBC 324, 100% lymphocytes</td>
<td>Granulomatous nodules involving serosal surface of bowel and diaphragm with yeast consistent with <em>B. dermatitidis</em> <em>Blastomyces</em> immunodiffusion serology positive. Ascitic fluid fungal cultures without growth. Patient was initially misdiagnosed as having tuberculosis</td>
<td>Diagnostic laparotomy, ketoconazole × 9 months</td>
<td>Survived</td>
<td>Perez-Lasala et al. (10)</td>
<td></td>
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<td>5</td>
<td>F</td>
<td>33</td>
<td>New-onset ascites with fever and bloody vaginal discharge. These symptoms were preceded by pleural effusion, fevers, night sweats, and chest pain approximately 10 months earlier</td>
<td>No</td>
<td>CXR: Left pleural thickening; Abdominopelvic CT: ascites, large TOA</td>
<td>TOA adherent to uterus, right ovary, omentum</td>
<td>WBC 1150 (82% lymphocytes)</td>
<td>Cervical smear with broad-based budding yeast; endometrium, fallopian tube, TOA, and peritoneum with granulomatous inflammation and broad-based budding yeast – cultures grew <em>B. dermatitidis</em></td>
<td>Surgical debridement, hysterectomy, right salpingo-oophorectomy, omentectomy. Amphotericin B deoxycholate × 10 weeks (2 g total)</td>
<td>Survived</td>
<td>Bundy et al. (7), Murray et al. (9)</td>
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<td>6</td>
<td>F</td>
<td>64</td>
<td>Diarrhea and increased abdominal girth in patient whose husband had documented genitourinary blastomycosis</td>
<td>No</td>
<td>CXR: no pulmonary disease</td>
<td>TOA (fallopian tubes, ovaries)</td>
<td>Ascite fluid drained at time of surgery, no studies performed</td>
<td>TOA and nodular studding of visceral and parietal peritoneum. Granulomtous inflammation of endometrium, fallopian tubes, and peritoneum. Initially misdiagnosed as tuberculosis; however, retrospective analysis of uterine tissue and fallopian tube demonstrated <em>B. dermatitidis</em>. Patient was also found to have endometrial adenocarcinoma</td>
<td>Debridement of TOA, hysterectomy with salpingo-oophorectomy. No antifungal therapy</td>
<td>Survived</td>
<td>Craig et al. (15), Farber et al. (21)</td>
</tr>
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<td>7</td>
<td>M</td>
<td>31</td>
<td>New-onset ascites and partial intestinal obstruction in a patient with pulmonary and genitourinary blastomycosis for approximately 1 year’s duration</td>
<td>No</td>
<td>Not reported</td>
<td>Lungs, genitourinary tract</td>
<td>Not reported</td>
<td>Widespread granulomatous lesions involving the peritoneum at laparotomy and autopsy. Histopathology consistent with peritoneal blastomycosis</td>
<td>Not reported</td>
<td>Died</td>
<td>Busey (18)</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>27</td>
<td>Pulmonary blastomycosis of 9 months’ duration. Abdominal pain, menorrhagia, metorrhagia</td>
<td>No</td>
<td>CXR: bilateral lung consolidation</td>
<td>Lungs, endometrium, cervix, bilateral fallopian tubes, ovaries, and probable vertebral osteomyelitis</td>
<td>4 L of ascitic fluid drained, no studies performed</td>
<td>Culture of sputum, endometrium, both TOAs, and nodules involving pelvic parietal peritoneum, omentum and intestine grew <em>B. dermatitidis</em>. Serum complement fixation positive</td>
<td>Surgical debridement of TOAs, hysterectomy, No antifungal therapy</td>
<td>Survived</td>
<td>Hamblen et al. (17), Martin &amp; Smith (23)</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>Not reported</td>
<td>Pulmonary and cutaneous blastomycosis</td>
<td>No</td>
<td>CXR: bilateral lung consolidation</td>
<td>Lungs, skin, lymph nodes, liver, spleen, kidney, omentum</td>
<td>Not reported</td>
<td>Caseating nodules involving the peritoneum at autopsy. Lungs tissue with <em>B. dermatitidis</em> yeast on smear</td>
<td>No antifungal therapy</td>
<td>Died</td>
<td>Coupal (22)</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>32</td>
<td>Disseminated blastomycosis of 2 years’ duration</td>
<td>No</td>
<td>Not reported</td>
<td>Lungs, spleen, appendix, lymph node, skin, subcutaneous tissue, and peritoneum</td>
<td>Not reported</td>
<td>Peritoneal involvement consistent with disseminated blastomycosis identified at autopsy</td>
<td>No antifungal therapy</td>
<td>Died</td>
<td>Wade &amp; Bel (24)</td>
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**Table 1 Continued**

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<tbody>
<tr>
<td>11</td>
<td>M</td>
<td>25</td>
<td>Disseminated blastomycosis of 9 months' duration</td>
<td>No</td>
<td>Not reported</td>
<td>Lungs, pleura, liver, spleen, kidney, adrenal, peritoneal, prostate, esophagus, skin, bone</td>
<td>Not reported</td>
<td>Peritoneal involvement consistent with disseminated blastomycosis at autopsy. Diffuse, small nodules involved the peritoneum, omentum, and capsules of spleen and liver</td>
<td>No antifungal therapy</td>
<td>Died</td>
<td>Wade &amp; Bel (24)</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>26</td>
<td>Disseminated blastomycosis for approximately 1 year's duration</td>
<td>No</td>
<td>Not reported</td>
<td>Lungs, pericardium, spleen, kidney, pancreas, peritoneum, skin, lymph node</td>
<td>Not reported</td>
<td>Miliary studding of peritoneum consistent with disseminated blastomycosis at autopsy</td>
<td>No antifungal therapy</td>
<td>Died</td>
<td>Wade &amp; Bel (24)</td>
</tr>
</tbody>
</table>

1Potassium iodine and/or vaccine therapy were administered.

CT, computed tomography; PR, present report; LUQ, left upper quadrant; CXR, chest x-ray; RUQ, right upper quadrant; WBC, white blood cells; LDH, lactate dehydrogenase; RBC, red blood cells.

Table 1
as basiliximab, for induction immunosuppression has not been associated with an increased incidence of fungal infection (4). Other opportunistic infections have been observed in SOT recipients with blastomycosis, most notably CMV (1).

Abdominopelvic infection with B. dermatitidis is an uncommon manifestation of disseminated disease and can involve almost any organ including the liver, gallbladder, large intestine, ovaries, spleen, and pancreas (5–11). The prostate is the most commonly affected abdominopelvic organ, with an incidence of <10% in several large case series (12, 13). In contrast, peritonitis from B. dermatitidis is rare. Clinical manifestations can include fever, night sweats, weight loss, abdominal pain, and increased abdominal girth from new-onset ascites (8, 10, 14, 15). Peritoneal blastomycosis is often associated with tubo-ovarian abscess or involvement of abdominal organs such as the spleen (8, 9, 14, 16, 17). Nodular studding of the omentum, bowel, and peritoneum is frequently observed at laparotomy or laparoscopy (8, 10, 14, 15, 18). Ascitic fluid white blood cell counts range from 4 to 1150 cells/mm³ commonly with a lymphocyte predominance (7, 10, 14). The patient reported herein had neutrophilic ascites, which has been described in Histoplasma peritonitis (19, 20).

The presence of concomitant pulmonary infection is variable. In 11 well-described cases of blastomycotic peritonitis (Table 1; 7–10, 14, 15, 17, 18, 21–24), 6 persons had definite pneumonia (17, 22, 24), and 3 had probable antecedent pulmonary infection (pleural thickening, pleural effusion) (7, 8, 14).

Peritonitis caused by other dimorphic fungi (Histoplasma capsulatum, Coccidioides immitis, and Coccidioides posadasii) and opportunistic fungi (Cryptococcus, Aspergillus) have been diagnosed in patients following solid organ transplantation, undergoing continuous ambulatory peritoneal dialysis (CAPD) for ESRD, hepatic allograft transplant candidates with cirrhosis, and in persons without known immunocompromise. Peritoneal histoplasmosis and coccidioidomycosis can occur in immunosuppressed patients (SOT, acquired immunodeficiency syndrome [AIDS]) with disseminated disease or in those receiving CAPD (25–30). Peritonitis from disseminated disease can be acute or indolent, and is characterized by abdominal pain with or without ascites, fever, chills, and anorexia. CAPD peritonitis from H. capsulatum or Coccidioides species is characterized by fever, abdominal pain, abdominal distension, and cloudy dialysate fluid (200–2133 cells/mm³) with a neutrophilic or eosinophilic predominance, respectively (19, 20, 31–34). An unusual manifestation of coccidioidal peritonitis is an enlarging inguinal hernia, which occurs in 30% (28, 30). Approximately 50% of patients with peritonitis from Coccidioides species have antecedent or concomitant pulmonary coccidioidomycosis (30). Peritonitis is one of the most common clinical manifestations of disseminated cryptococcosis in patients with cirrhosis (35, 36). Cryptococcal meningitis occurs in 65–71% and meningitis in 20% (37, 38). Although cryptococcal peritonitis is predominately associated with cirrhosis, it can occur in patients with AIDS or ESRD on CAPD (37, 38). In contrast, Aspergillus fumigatus peritonitis primarily occurs in patients undergoing CAPD, however, it can occur following solid organ transplantation (39).

Diagnosis of peritoneal blastomycosis requires a high index of suspicion. Serum or urinary Blastomyces antigen tests are likely to be positive in disseminated disease. The utility of testing peritoneal fluid by the Blastomyces antigen enzyme immunoassay is unknown. Fungal cultures of peritoneal fluid or peritoneal tissue remain the gold standard. CT imaging findings suggestive of disseminated fungal infection involving the peritoneum include nodularity and peritoneal thickening. Antifungal treatment regimens for peritoneal blastomycosis should be based on the Infectious Diseases Society of America guidelines and include a lipid formulation of amphotericin B or azole antifungal (40). Intraperitoneal instillation of antifungals is not needed.

**Conclusion**

In conclusion, peritonitis caused by B. dermatitidis is an uncommon complication following solid organ transplantation. Patients with peritoneal involvement – both SOT recipients and non-SOT recipients – can present with fevers, abdominal pain, and ascites. Concomitant or antecedent pneumonia occurs in at least half the cases. A high index of suspicion is necessary to diagnose fungal peritonitis in SOT patients who present with new-onset ascites. Evaluation should include serum or urine antigen testing, fungal culture of ascitic fluid (and peritoneal tissue at laparotomy), fungal culture of extra-abdominal sites of infection, diagnostic testing for opportunistic co-infections (e.g., CMV), and imaging to identify extra-peritoneal sites of infection. Optimal treatment requires antifungal therapy and debridement of abdominopelvic abscesses.

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**Author contributions:** J.A.B. & G.M.G.: Participated in concept, design, data analysis, writing, critical revision, and approval of article.
References


