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# A Case of Gastrointestinal Coccidiomycosis With Bowel Perforation Secondary to Relapsing DLBCL

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## Abstract

*Coccidioides* is a fungus endemic to the Southwestern United States, known for causing Valley Fever. While typically asymptomatic or presenting as a respiratory tract infection, rare cases of disseminated infection to the peritoneum have been reported. The patient in this case study presented with a small bowel obstruction, requiring an exploratory laparoscopy showing evidence of an inflammatory mass with a jejuna-colic fistula with adherence to the spleen. The patient underwent splenectomy with a cholecystectomy and small bowel resection. Intraabdominal cultures revealed *Coccidioides*, and so he started long-term antifungal treatment. The patient was also initiated on salvage chemotherapy for DLBCL, and ultimately received CAR T-Cell therapy at a tertiary center. This case report highlights a unique presentation of gastrointestinal *Coccidioides* infection, in the setting of an immunocompromised host with a hematologic malignancy. It also provides insight into the therapeutic challenges clinicians face when treating complicated patients such as this who require urgent chemotherapy while risking further immunosuppression in the setting of active infection.

**Keywords:** *Coccidioides*, CAR T-cell therapy, Small bowel obstruction

## 1. Introduction

Diffuse large B-cell lymphoma (DLBCL) is a subtype of Non-Hodgkin Lymphoma (NHL) that is aggressive, highly proliferative, and fatal if left untreated.<sup>1</sup> The clinical presentation is often heterogeneous and depends on the site of origin of the malignancy. Extra-nodal involvement can be seen in one-third of cases, with the most common site being the GI tract.<sup>2</sup> B symptoms such as fever, night sweats, and weight loss are typically present. Still, it can be challenging to diagnose initially, and it is often accompanied by associated complications such as bowel obstruction, etc.<sup>3</sup> Forty percent of patients with DLBCL can relapse after completing therapy, which carries a poorer prognosis.<sup>4</sup> Therapy typically consists of a combination chemotherapy regimen consisting of either rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) or rituximab, etoposide, prednisone,

vincristine, and cyclophosphamide (R-EPOCH) depending on the patient population.<sup>5</sup>

Due to immune system compromise, patients on chemotherapy with DLBCL have increased morbidity and mortality from infections. Among the various agents, fungal infections comprise 19% of those infections.<sup>6</sup> *Coccidioides* is a dimorphic fungus found ubiquitously in the soil in the Southwestern United States and is responsible for the development of Valley Fever.<sup>7</sup> It primarily infects the host through the lungs, when the spores are inhaled, but it can be a disseminated infection.<sup>7</sup> While rare, *Coccidioides* can involve the peritoneum, with several case reports demonstrating the diverse clinical presentations that can manifest in such cases, ranging from no symptoms to severe abdominal pain and small bowel obstruction.<sup>8</sup> We present a unique case of gastrointestinal *Coccidioides* with bowel perforation and jejuna-colic fistula with adherence to spleen secondary to DLBCL.

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## 2. Case presentation

A 67-year-old male presented for evaluation of intense mid-epigastric abdominal pain with an unintentional 18-pound weight loss over 3-weeks. He had a history of DLBC, which was treated 3 years prior with R-EPOCH with intrathecal (IT) methotrexate for 6 cycles of chemotherapy and was currently in remission. He also reported a recent history of unexplained small bowel obstruction that was resolved with nasogastric (NG) tube placement. His examination was remarkable for dry mucosal membranes and mid-epigastric tenderness on palpation.

There was concern for small bowel obstruction, and therefore a small bowel series was ordered, revealing a 7 cm narrowing in the body of the stomach near the pylorus (Fig. 1). The patient had an endoscopy 2 weeks prior for similar symptoms, which was negative for any abnormalities. Due to persistent abdominal pain and concern for underlying malignancy, he received an MRCP, HIDA scan, and CT abdominal angiogram, which were unremarkable. He continued to have persistent postprandial abdominal pain and multiple episodes of diarrhea and therefore underwent exploratory laparoscopy. The procedure was converted to open cholecystectomy with small bowel resection and splenectomy due to findings of an edematous gallbladder with fistula formation between the proximal jejunum, splenic flexure of the colon, and densely adherent spleen. He was also found to have an inflammatory mass in the left upper quadrant, with tissue biopsy results revealing evidence of recurrent high-grade B-cell lymphoma.

Additionally, Intra-abdominal cultures were positive for polymicrobial infection and was started on empiric meropenem and micafungin due to



Fig. 1. 7cm narrowing in the body of the stomach near the pylorus.

persistently elevated leukocytosis on Zosyn. A post-operative CT abdomen pelvis showed evidence of an  $11 \times 6 \times 14$  cm abscess in the left upper quadrant, requiring an intra-abdominal percutaneous drainage (Fig. 2). Cultures from the intra-abdominal abscess drain returned positive for *Coccidioides*, with serology consistent with *Coccidioides immitis* infection. The patient revealed that he traveled frequently to Arizona to visit family. He was also noted to have a longstanding calcified granuloma in the right lower lobe on CT chest, suggesting the source of his gastrointestinal *Coccidioides* infection. The patient started IV voriconazole and was later transitioned to IV fluconazole. Repeat CT imaging showed interval improvement of the abscess, and the patient was transitioned to Unasyn. Oncology was also consulted for the DLBC, who initiated salvage chemotherapy after the infection was controlled with gemcitabine-oxaliplatin plus rituximab. The patient's condition continued to improve, and he received asplenia vaccines, including HIB, PCV 13, influenza, quadrivalent meningococcal vaccine (MenQuadfi), and meningococcal B vaccine. He was discharged on IV fluconazole 400 mg daily, with total parenteral nutrition for his severe malnutrition and inability to tolerate oral intake post-surgery.

In the interim, the patient had recurrent intra-abdominal abscess and was resumed on long-term IV antibiotic therapy with meropenem. He followed up at a tertiary care center, where he received CART T-cell extraction, and was transitioned to oral fluconazole as

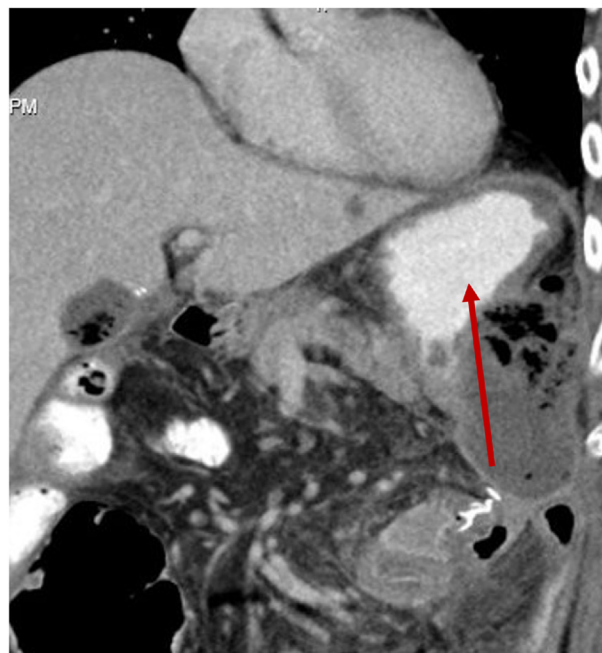


Fig. 2.  $11 \times 6 \times 14$  cm abscess in the left upper quadrant.

his intra-abdominal sinus tract healed. After 3 months, the patient also received axicabtagene ciloleucel therapy, and will continue fluconazole until one year from his CAR T-cell therapy.

### 3. Discussion

This case report demonstrates a complex case presentation of gastrointestinal Coccidioidomycosis infection with a concurrent jejunum-colic-splenic fistula secondary from relapsing DLBCL. In our case, the patient likely contracted *Coccidioides* during his visit to Arizona and developed a latent infection as evidenced by the granuloma seen on CT. Cellular immunity through the activation of T-helper cells such as TH1 and TH17 is vital for the clearance of fungi such as coccidioidomycosis.<sup>9</sup> Thus, when our patient received treatment for the DLBCL with R-EPOCH, he likely reactivated the latent infection, leading to hematogenous dissemination and GI involvement. Once the patient's immune system recovered after chemotherapy he cleared the fungemia, as the initial blood cultures were negative when the patient presented to the ED this admission. Active infection with an intraabdominal abscess made management challenging, as treating the underlying malignancy would further weaken his immune system in fighting off the fungal infection.

DLBCL has an excellent response to therapy, as prompt chemotherapy can be curative in two-thirds of patients. Patients who relapse often have worse outcomes and previously were treated with salvage chemotherapy and autologous stem cell transplantation (ASCT). Five recent studies have shown evidence of CAR T-cell therapy as an effective third-line agent, with some evidence even showing it superior to traditional salvage chemotherapy/ASCT.<sup>10–12</sup> CAR T cell therapy is a multistage process that requires weeks of processing the host T cells for CD19 targeting. There is typically a bridging period with the inclusion of glucocorticoids for rapidly proliferative disease.<sup>13</sup> Our case was further complicated by the findings of *C. immitis* positive culture in the intraabdominal mass, suggesting previous disseminated hematogenous spread. While repeat blood cultures were negative, there was concern that if bridging therapy with glucocorticoids was pursued, it would potentiate reactivation of underlying *Coccidioides* or other opportunistic infections. Therefore, before initiating treatment with lymphodepleting chemotherapy, one must screen with serologic testing, starting with enzyme-linked immunoassay for immunoglobulin M (IgM) and immunoglobulin G (IgG).<sup>14</sup> These combined tests are highly sensitive (94.8%) and if positive it should

prompt clinicians to get immunodiffusion and complement-fixation testing as they are more specific.<sup>15</sup>

In our patient's case, any delay of CAR T-cell therapy would have led to increased morbidity and mortality, as the patient's recurrent lymphoma was contributing to the obstructive and septic symptoms. Accordingly, treating the underlying cause is the only way to ensure that these symptoms do not return. Even after patients receive CAR T-cell therapies, they continue to be at high risk for opportunistic infections. Case studies of disseminated coccidioidomycosis have been documented due to IgG suppression and lymphopenia because of CAR T-Cell therapy, making management challenging and requiring consistent follow-up with more long-term antifungal treatment in patients living in endemic regions.<sup>16</sup>

In conclusion, for patients with diffuse or mid-epigastric pain with negative radiographic findings or diagnostic studies, one should consider the possibility of underlying extra-nodal GI lymphoma. In our case, exploratory laparotomy led to the timely diagnosis and identification of the etiology of the patient's symptoms, and chemotherapy was pursued along with CAR-T cell therapy for curative intent, along with concurrent treatment of gastrointestinal coccidioidomycosis.

### Ethics information

All patient identifying information where removed from this paper in accordance with HIPAA compliance, and consent was obtained prior to publication.

### Author contribution

All authors participated in the planning, research, drafting, and editing portions of this case report.

### Disclaimers

This case report has not been published anywhere prior.

### Data availability

All data was obtained from EMR from Healthcare System. All protected health information was withheld from publication per HIPAA Privacy Rules.

### Source of support

There was no financial support, equipment, or competing interests for this case report.

### Conflicts of interest

No conflict of interest to disclose for all parties.



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