

# A Rare Case of Systemic Adult Burkitt Lymphoma Presenting as Acute Acalculous Cholecystitis

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## ABSTRACT

Acute acalculous cholecystitis (AAC) is an uncommon presentation of cholecystitis accounting for 10% of cases. AAC is caused by a localized ischemic event in the gallbladder usually in critically ill patients. Several cases of localized or systemic lymphoma have been described in the literature as causes of AAC. We present a patient with a rare case of AAC due to undiagnosed systemic Burkitt lymphoma. Pathology of the gallbladder revealed Burkitt lymphoma with analysis of his cerebral spinal fluid confirming Stage IV disease. This case report reviews acute acalculous cholecystitis, lymphomas of the gallbladder and extrahepatic duct, and adult Burkitt lymphoma.

## INTRODUCTION

Acute acalculous cholecystitis (AAC) is associated with high morbidity and mortality and represents approximately 10% of all cases of acute cholecystitis. AAC is commonly observed in critically ill patients and is associated with shock, total parenteral nutrition, infections, burns, and trauma.<sup>1,2</sup> Sporadic adult Burkitt lymphoma accounts for 1%–2% of all adult lymphomas in Western Europe and the United States.<sup>3,4</sup> Patients with widespread lymphoproliferative disease with secondary infiltration of the gallbladder is unusual.<sup>5</sup> We present an extremely rare case of AAC due to sporadic adult Burkitt lymphoma.

## CASE PRESENTATION

A 65-year-old white man presented to the emergency department complaining of abdominal pain and bloating. Abdominal computed tomography demonstrated findings consistent with cholecystitis and pancreatitis. He was treated for acute pancreatitis and discharged with 7 days of ciprofloxacin and metronidazole therapy. Pancytopenia was noted, and he was scheduled for a bone marrow biopsy.

The patient returned 3 weeks later for worsening symptoms despite antibiotic compliance endorsing weight loss, polydipsia, lightheadedness, fatigue, dyspnea on exertion, and bruising. The patient denied recent alcohol use. Vital signs were normal except for a blood pressure of 153/89 mm Hg. On physical examination, he had mild abdominal distention and +1 pitting edema in his lower extremities bilaterally.

A comprehensive metabolic profile showed hyponatremia 134 mmol/L, anion gap 12 mEq/L, blood urea nitrogen 25 mg/dL, creatinine 1.8 mg/dL, patient's baseline creatinine 1.0 mg/dL, total bilirubin 0.7 mg/dL, AST 52 IU/L, ALT 37 U/L, alkaline phosphatase 85 U/L, total protein 6.3 g/dL, albumin 2.9 g/dL, lactate 4.2 mmol/L, lactate dehydrogenase 626 U/L, and lipase 1,145 U/L. His blood counts revealed the following: hemoglobin 9 g/dL, hematocrit 28.4%, white blood cell count 2.9 K/mm<sup>3</sup>, 49% segmented neutrophils, 7% bands, and platelet count 78 K/mm<sup>3</sup>. Serum protein electrophoresis revealed hypogammaglobulinemia and hypoalbuminemia. Quantitative polymerase chain reaction was negative for BCR-ABL 1 transcripts.

Abdominal and pelvic computed tomography revealed diffuse abdominal inflammation, gallbladder distention with wall thickening, pericholecystic fluid, and inflammation of the pancreas concerning for pancreatitis (Figure 1). Ultrasound revealed sludge, positive sonographic Murphy sign and pericholecystic fluid without cholelithiasis consistent with likely cholecystitis. The patient was started on piperacillin/tazobactam and emergently taken for cholecystectomy due to shock. Intraoperatively, the gallbladder and duct system appeared grossly abnormal; histologic evaluation revealed large lymphoid cells and a starry sky pattern. Immunohistochemistry study of c-MYC CD20 and Pax-5 stains was positive for CD10, BCL-6, and high Ki-67 proliferation rate at 100% (Figure 2). Fluorescence in situ hybridization analysis was positive for MYC gene rearrangement and gain of chromosome 14 (Figure 3).

Lumbar puncture demonstrated white blood cells of 310 cells/mm<sup>3</sup> and protein of 1,715 mg/dL. Smear of the cerebral spinal fluid showed malignant cells and immature lymphoid cells with cytoplasmic vacuoles, consistent with Burkitt lymphoma. Flow cytometry was positive for malignant cells, which were lambda+, CD10+, CD19+, CD20+, CD22+ c-MYC+, CD34-, and TdT with reduced expression of CD45. Immunohistochemistry of the cerebrospinal fluid revealed BCL6+, BCL2-, CD10+, CD20+, cMYC+, CD34-, TdT-, and Ki67 100%. The patient was treated with EPOCH (etoposide, vincristine, doxorubicin, and prednisone) and rituximab as chemotherapy.

## DISCUSSION

Acute acalculous cholecystitis (AAC) is an acute necroinflammatory condition of the gallbladder. AAC is associated with a mortality rate of 30% related to a 50% prevalence of gangrene and a 10% incidence of perforation.<sup>2</sup> Postoperative AAC occurs with male predominance, over 80% of cases. AAC is associated with chronic conditions such as vasculitis, congestive heart

failure, diabetes mellitus, and chronic kidney disease.<sup>6,7</sup> Gallbladder ischemia plays an important role in the pathogenesis of AAC. In addition, there is an association with stasis related to states of hypoperfusion, such as sepsis and hypotension.<sup>8</sup>

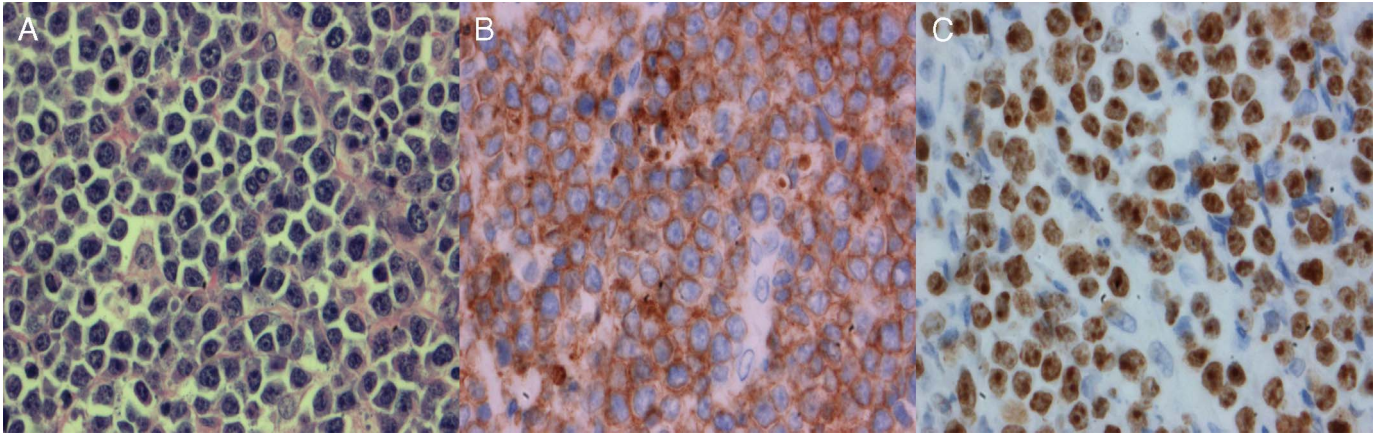
Ultrasonography or computed tomography is usually performed initially in patients with suspected acute abdomen, with thickening of the gallbladder wall being the most reliable sign of AAC.<sup>9,10</sup> Early appropriate antibiotic therapy is important to ensure a favorable outcome.<sup>1,11,12</sup> Generally, a cholecystectomy is indicated; however, in high-risk surgical patients, percutaneous or endoscopic drainage may be warranted.<sup>8,11,13</sup>

When AAC is caused by a mass arising from the gallbladder or extrahepatic duct, the distinction between gallbladder adenocarcinoma and lymphoma is difficult to achieve without histological confirmation, as was the case with our patient.<sup>2,5</sup> On computed tomography, low-grade lymphomas may present as a slight thickening in the gallbladder wall, whereas high-grade lymphomas tend to form a solid mass or irregular thickening in the wall, but this patient did not have a solid mass more indicative of high-grade lymphoma.<sup>14</sup> Because of a low incidence rate, histopathology should only be performed in patients with suspected malignancy because it would not be cost-effective.<sup>15</sup> Once diagnosed with lymphoma, all patients should have a complete staging workup to guide treatment options.

Lymphomas of the gallbladder and extrahepatic duct are extremely rare, with most cases reported in the literature presenting with symptoms of cholecystitis.<sup>16</sup> This patient's AAC was likely in the setting of significant hypoperfusion in the setting of shock and less likely malignancy. Adult Burkitt lymphoma has 3 clinical variants: endemic, immunodeficiency, and sporadic.<sup>3</sup> Sporadic Burkitt lymphoma accounts for 1%–2% of all adult lymphomas in the United States and Western Europe, typically patients with sporadic variant present with extranodal disease in the abdomen.<sup>3,4,17</sup>



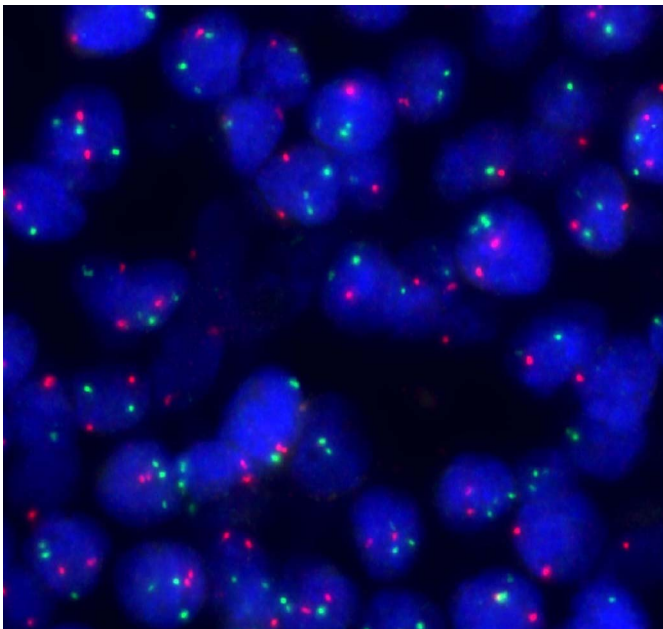
**Figure 1.** Coronal plane abdominal computed tomography showing (A) generalized increasing diffuse abdominal inflammation with small volume perihepatic fluid along with gallbladder distension, wall thickening, and pericholecystic fluid consistent for acute cholecystitis (arrows), and (B) no evidence of common biliary duct obstruction (arrow).



**Figure 2.** (A) Hematoxylin and eosin stain revealed gallbladder tissue with extensive involvement by monotonous large lymphoid cells with fine chromatin with frequent mitosis. CD20 and Pax-5 stains highlight sheets of neoplastic B cells that are also positive for (B) CD10, BCL-6, and (C) a high Ki-67 proliferation rate at 100%.

Burkitt lymphoma is associated with a translocation of the site of the *c-MYC* oncogene between the long arm of chromosome 8 with 1 of 3 locations on immunoglobulin genes: kappa light chain gene on chromosome 2, immunoglobulin heavy chain gene on chromosome 14, and lambda light chain gene on chromosome 22.<sup>18</sup> Our patient had a rare triple-hit B-cell lymphoma with high expression of *c-MYC*, coupled with BCL-2, and BCL-6, both being positive.<sup>19</sup> Chemotherapy remains the mainstay of treatment in Burkitt lymphoma.

Lymphomas of the gallbladder and extrahepatic duct are rare causes of acute acalculous cholecystitis. Histological



**Figure 3.** Fluorescence in situ hybridization analysis showing an abnormal signal pattern in the MYC probe set in the 14;18 probe set indicative of a MYC gene rearrangement and gain of the IgH gene or chromosome 14, or an IgH rearrangement with a gene other than BCL2 on chromosome 18.

evaluation is important in cases of acute acalculous cholecystitis whenever malignancy is suspected. Once the diagnosis is made, the stage of the disease dictates the treatment plan. This case adds to the limited literature of systemic adult Burkitt lymphoma with the initial presentation of acute acalculous cholecystitis.<sup>20</sup>

## DISCLOSURES

Author contributions: B. Doherty wrote the manuscript and is the article guarantor. W. Palmer, J. Cvinar, and N. Sadek edited the manuscript.

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Informed consent was obtained for this case report.

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