Journal of Gastrointestinal Surgery (2019) 23:1589–1592
https://doi.org/10.1007/s11605-018-04077-w

ORIGINAL ARTICLE

Biliary Disease in Immunocompromised Patients: a Single-Center Retrospective Analysis

Justin George[1] · Marc Cohen[1] · Stewart Whitney[1] · Erin Fennern[1] · Celia Divino[1]

Received: 9 August 2018 / Accepted: 28 November 2018 / Published online: 11 January 2019

Abstract

Background Acute cholecystitis is a life-threatening disease process in immunocompromised patients. The purpose of this study is to determine the incidence, clinical course, and management of calculous and acalculous acute cholecystitis in immunocompromised patients.

Methods A single center's database was queried for all patients with a diagnosis of acute cholecystitis from January 1, 2003 to September 30, 2016 with concomitant diagnosis of neutropenia, leukopenia, leukemia, or lymphoma. These cases subsequently underwent chart review. Data on demographics, diagnostic studies, and management were collected and analyzed.

Results There were 4525 patients diagnosed with acute cholecystitis during the study window. One hundred twenty patients were identified to be immunocompromised at time of diagnosis. Seventy-nine patients (65.8%) had acute calculous cholecystitis while 41 patients (34.2%) had acalculous cholecystitis. There were no significant demographic differences between calculous and acalculous groups. There was similar use of percutaneous cholecystostomy tube (7.6%, 9.8%, $p = 0.69$), laparoscopic cholecystectomy (70.9%, 61.0%, $p = 0.27$), and open cholecystectomy (10.3%, 2.4%, $p = 0.13$) in both calculous and acalculous groups.

Discussion While immunosuppression is commonly thought to be associated with acalculous cholecystitis, our data suggest the majority of acute cholecystitis in immunocompromised patients are calculous. Most patients in our studies were managed successfully with laparoscopic cholecystectomy with acceptably low complication rates.

Conclusion Calculous cholecystitis is more common than acalculous cholecystitis in immunocompromised patients. Both are often managed successfully with laparoscopic cholecystectomy with very low rates of conversion to open cholecystectomy.

Keywords Immunocompromised · Biliary · Cholecystitis · Calculous · Acalculous

Introduction

Acute cholecystitis may present as a potentially life threatening illness in immunocompromised patients. This disease process is often subdivided into calculous and acalculous cholecystitis. Acute calculous cholecystitis is defined as inflammation of the gallbladder caused by cystic duct obstruction due to gallstones or biliary sludge. Alternatively, acute acalculous cholecystitis is inflammation of the gallbladder without cystic duct obstruction.

Acute acalculous cholecystitis accounts for 2–10% of all cases of acute cholecystitis with some studies suggesting an increasing incidence.[1–4] The pathophysiology is different from calculous cholecystitis and thus usually affects a different patient population. There have been reports of opportunistic organisms causing primary infections of the gallbladder suggesting a possible pathophysiology for acalculous cholecystitis in the immunocompromised patients.[5,6] Additional small case reports have shown CMV to be precipitating factor for development of acalculous acute cholecystitis in severely immunodeficient patients.[7,8]

The acalculous variant is thought to be associated with critically ill patients and seen in various clinical settings including severe trauma, burns, low perfusion states, recent surgery, and immunosuppression.[9,10] Given this association with significantly ill patients, acute acalculous cholecystitis is thought to be associated with a higher mortality rate than acute calculous cholecystitis.[11]

✉ Celia Divino
Celia.Divino@mountsinai.org

[1] Mount Sinai Department of General Surgery, Icahn School of Medicine at Mount Sinai, 5 East 98th Street, 15th floor, New York, NY 10029, USA

The management of acute cholecystitis in immunocompromised patients can be quite challenging. Previous studies have endorsed laparoscopic cholecystectomy in healthy patients while suggesting percutaneous cholecystostomy in patients who are poor surgical candidates; however, these recommendations were not specific to immunocompromised patients.[3]

There is a scarcity of data on acute cholecystitis in immunocompromised patients, particularly in the management of acute acalculous cholecystitis in this subgroup. The purpose of this study is to evaluate the incidence, clinical course, management, and outcomes of acute calculous and acalculous cholecystitis in immunocompromised patients.

Methods

An Institutional Review Board waiver was obtained for this study. A single center's database was queried for all patients with a diagnosis of acute cholecystitis from January 1, 2003 to September 30, 2016. Patients less than 18 years of age or AIDS were excluded from the study. The query was performed using ICD-9 and ICD-10 codes to capture acute cholecystitis, acute acalculous cholecystitis, and acute calculous cholecystitis. These cases were then filtered for concomitant diagnosis of neutropenia, leukopenia, leukemia, or lymphoma. The remaining filtered cases subsequently underwent chart review to ensure simultaneous active diagnoses of cholecystitis and immunosuppression. A diagnosis of calculous or acalculous cholecystitis were confirmed by reviewing sonographic and nuclear medicine studies. Pathology reports for all operative cases were reviewed. Data on demographics, management, and outcomes including surgical management and complications were collected and analyzed using SPSS (IBM SPSS Statistics, last version used: 23.0; Armonk, NY, USA, IBM Corp.).

Results

A total of 4525 patients were diagnosed with acute cholecystitis during the study window. Of these, 120 patients were identified to be immunocompromised at the time of diagnosis with 97 (80.8%) having leukemia or recent bone marrow transplantation resulting in neutropenia. Seventy-nine patients (65.8%) were found to have acute calculous cholecystitis while 41 patients (34.2%) were found to have acalculous cholecystitis.

There was no significant difference between calculous and acalculous groups in age (62.4 ± 16.5, 59.9 ± 17.4, $p = 0.46$), male gender (46.8%, 51.2%, $p = 0.65$), exposure to blood transfusion before diagnosis (36.7%, 36.6%, $p = 0.99$), concomitant diagnosis of graft verse host disease (3.8%, 4.9%, $p = 0.78$), or CMV seropositive status (11.4%, 12.2% $p = 0.90$) (Table 1).

There was similar use of percutaneous cholecystostomy drainage in calculous and acalculous cholecystostomy groups (7.6%, 9.8%, $p = 0.69$). There was no statistically significant difference in proportion of patients undergoing laparoscopic cholecystectomy (70.9%, 61.0%, $p = 0.27$) or open cholecystectomy (10.3%, 2.4%, $p = 0.13$) between calculous and acalculous groups (Table 2). There were a total of 12 cases of gangrenous cholecystitis, 6 in the calculous group and 6 in the acalculous group.

Immunocompromised patients who underwent laparoscopic cholecystectomy required conversion to an open procedure in four cases (4.9%). The 30-day morbidity and mortality rate for the laparoscopic cholecystectomy group was 7.4% and 2.5% respectively. This included two cases of pulmonary embolism (2.4%), one case of myocardial infarction (1.2%), three cases requiring 30-day re-admission (3.7%) (Table 3).

Discussion

Abdominal infections are a life-threatening condition in immunocompromised patients. Acute cholecystitis has previously been described in this patient population. Prior studies have found an incidence of 0.4% of cholecystitis in patients undergoing aggressive myelosuppressive chemotherapy with 2/3 having acute acalculous cholecystitis.[12] In patients with acute leukemia, 1.65% developed acute acalculous cholecystitis.[10] While immunosuppression is commonly thought to be associated with acalculous cholecystitis, our data suggest the majority of acute cholecystitis in immunocompromised patients are actually calculous. Nearly two thirds of the

Table 1 Characteristics of immunocompromised patients with acute calculous and acalculous cholecystitis

Characteristics	Total ($n = 120$)	Calculous ($n = 79$)	Acalculous ($n = 41$)	p value
Age (avg ± std)	61.5 ± 16.9	62.4 ± 16.5	59.9 ± 17.4	0.46
Male	48.3% (59)	46.8% (38)	51.2% (21)	0.65
TPN Use	18.3% (22)	16.5% (13)	22.0% (9)	0.46
Blood Transfusion	36.7% (44)	36.7% (29)	36.6% (15)	0.99
GVHD	4.2% (5)	3.8% (3)	4.9% (2)	0.78
CMV seropositivity	11.7% (14)	11.4% (9)	12.2% (5)	0.90

Table 2 Management of immunocompromised patients with acute calculous and acalculous cholecystitis

Intervention	Total ($n = 120$)	Calculous ($n = 79$)	Acalculous ($n = 41$)	p value
Percutaneous cholecystostomy	8.3% (10)	7.6% (6)	9.8% (4)	0.69
Laparoscopic cholecystectomy	67.5% (81)	70.9% (56)	61.0% (25)	0.27
Intraoperative cholangiogram (of patient undergoing lap chole)	40.7% (33)	37.5% (21)	48.0% (12)	0.70
Open cholecystectomy	7.6% (9)	10.3% (8)	2.4% (1)	0.13

immunocompromised patients in our study demonstrated sonographic findings consistent with calculous cholecystitis.

The literature suggests an increased proportion of acalculous cholecystitis is secondary to risk factors unique to the immunocompromised population. Prior studies have suggested blood transfusion, GVD, and CMV seropositivity were linked with acalculous cholecystitis;[5–8] however, our data demonstrate the presence of these risk factors were similar in both calculous and acalculous groups. We surmise that while acalculous cholecystitis is more likely to occur in an immuncompromised patient, the overall incidence of the calculous variant is still higher.

Treatment for acute cholecystitis in immunocompromised patients is dependent on the patient's clinical status. Percutaneous cholecystostomy is the treatment option of choice for critically ill patients with acute cholecystitis while more stable patients may undergo definitive laparoscopic cholecystectomy.[3,13] Studies have demonstrated percutaneous cholecystostomy resulted in clinical improvement in 86% of patients.[14] There was no clear algorithm in our study for percutaneous cholecystostomy tube vs laparoscopic cholecystectomy, rather this decision was based primarily on the patient's clinical status and surgical attending judgment. More than 2/3 of patients in our series were safely treated with initial laparoscopic cholecystectomy with only 4 cases requiring conversion to open cholecystectomy. There were no common bile duct injuries and acceptably low complication rate. Of note, there were 12 cases of gangrenous cholecystitis in our study, 6 in the calculous group and 6 in the acalculus group. Many of these patients were critically ill; however, all underwent laparoscopic cholecystectomy. The majority of these gangrenous cholecystitis cases recovered well postoperatively and were eventually discharged with only 1 case resulting in a 30-day mortality. Our study demonstrates that laparoscopic cholecystectomy is safe and effective for the treatment of both calculous and acalculous cholecystitis in the immunocompromised population.

The data in our study span a decade in which there have been marked improvement in equipment, surgeon comfort, and ultimately patient outcomes with laparoscopic surgery. Many of the open cholecystectomy and laparoscopic converted to open cholecystectomy cases occurred toward the beginning of the study period. We anticipate further improvement in outcomes for immunocompromised patients undergoing laparoscopic cholecystectomy. Furthermore, while our study primarily focuses on biliary disease in immunocompromised patients, patients with AIDs were excluded from our study. This was done in order to prevent erroneously including patients with HIV cholangiopathy. AIDs remains a cause of immunocompromised biliary disease; however, we feel that our data is still generalizable to the remainder of the immunocompromised community.

Table 3 Outcomes of immunocompromised patients with acute cholecystitis undergoing laparoscopic cholecystectomy

Characteristics and outcomes ($n = 81$)	% (n)
Calculous cholecystitis	69.1% (56)
Acalculous cholecystitis	30.9% (25)
Previous percutaneous cholecystostomy tube	3.7% (3)
Retained stones	13.6% (11)
CBD injury	0.0% (0)
Conversion to open	4.9% (4)
Pulmonary embolism	2.4% (2)
Myocardial infarction	1.2% (1)
Surgical site infection	7.7% (6)
Bile leak	0.0% (0)
30-day re-admission	3.7% (3)
30-day mortality	2.5% (2)

Conclusion

Calculous cholecystitis is more common than acalculous cholecystitis in immunocompromised patients. Both variants of acute cholecystitis are often managed successfully with laparoscopic cholecystectomy with very low rates of conversion to open cholecystectomy.

Authors' Contributions Dr. Justin George, Mr. Marc Cohen, Dr. Stewart Whitney, and Dr. Erin Fennern were involved in data acquisition, data analysis, and manuscript revision. Dr. Celia Divino was involved in supervising all aspects of the study including data acquisition, analysis, and critical revisions to the final manuscript. All authors discussed the results and contributed to the final manuscript.

References

1. Gu, M.G., et al., *Risk factors and therapeutic outcomes of acute acalculous cholecystitis.* Digestion, 2014. **90**(2): p. 75–80.
2. Nikfarjam, M., et al., *Outcomes of patients with histologically proven acute acalculous cholecystitis.* ANZ J Surg, 2012. **82**(12): p. 918–22.
3. Treinen, C., et al., *Acute acalculous cholecystitis in the critically ill: risk factors and surgical strategies.* Langenbecks Arch Surg, 2015. **400**(4): p. 421–7.
4. Savoca, P.E., et al., *The increasing prevalence of acalculous cholecystitis in outpatients. Results of a 7-year study.* Ann Surg, 1990. **211**(4): p. 433–7.
5. Landau, Z., et al., *Acute cholecystitis caused by Campylobacter jejuni.* Isr J Med Sci, 1995. **31**(11): p. 696–7.
6. Gomez, N.A., J. Gutierrez, and C.J. Leon, *Acute acalculous cholecystitis due to Vibrio cholerae.* Lancet, 1994. **343**(8906): p. 1156–7.
7. Ong, E.L., et al., *Cytomegalovirus cholecystitis and colitis associated with the acquired immunodeficiency syndrome.* J Infect, 1989. **18**(1): p. 73–5.
8. Adolph, M.D., et al., *Cytomegaloviral acalculous cholecystitis in acquired immunodeficiency syndrome patients.* Am Surg, 1993. **59**(10): p. 679–84.
9. Munster, A.M. and J.R. Brown, *Acalculous cholecystitis.* Am J Surg, 1967. **113**(6): p. 730–4.
10. Buyukasik, Y., et al., *Acalculous acute cholecystitis in leukemia.* J Clin Gastroenterol, 1998. **27**(2): p. 146–8.
11. Glenn, F. and C.G. Becker, *Acute acalculous cholecystitis. An increasing entity.* Ann Surg, 1982. **195**(2): p. 131–6.
12. Gorschluter, M., et al., *Cholecystitis in neutropenic patients: retrospective study and systematic review.* Leuk Res, 2006. **30**(5): p. 521–8.
13. Barie, P.S. and S.R. Eachempati, *Acute acalculous cholecystitis.* Gastroenterol Clin North Am, 2010. **39**(2): p. 343–57, **x**.
14. Noh, S.Y., et al., *Role of percutaneous cholecystostomy for acute acalculous cholecystitis: clinical outcomes of 271 patients.* Eur Radiol, 2018. **28**(4): p. 1449–1455.