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Biliary Drainage For Sepsis Control In Acute Cholangitis: A Case Report

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ORIGINAL

Abstract
Acute cholangitis leading to sepsis is a common occurrence, especially in populations with a high prevalence of gallstones. Unfortunately, the mortality rate related to this issue is high. Recently, we had a case involving an elderly woman who initially had mild acute cholangitis, but it progressed into a severe case. Respiratory and hematological issues developed, along with worsening septic parameters and liver functions. As a result, she was intubated, ventilated, and monitored in the intensive care unit (ICU). Urgent ERCP failed, but PTBD and percutaneous cholecystostomy were inserted to aid in biliary decompression and sepsis control. Currently, she is recovering from sepsis and plans for early ERCP and cholangiogram before definitive surgical intervention. To handle obstructed biliary sepsis, early biliary drainage is crucial for urgent biliary decompression and sepsis control, alongside fluid resuscitation, intravenous antibiotics, and intensive care.

Keywords : Percutaneous cholecystostomy, endoscopic nasobiliary drainage (ENBD), percutaneous transhepatic biliary drainage (PTBD), biliary decompression, endoscopic retrograde cholangiopancreatography (ERCP).

Introduction

Sepsis is a highly concerning medical condition that can lead to organ dysfunction due to the body's response to infection (1). This condition has a high mortality rate, affecting between one in three and one in six individuals (1). Acute cholangitis is a common biliary sepsis type that arises due to obstruction of the biliary system caused by a tumor or stone, leading to the accumulation of microorganisms as a result of increased pressure (2; 3). Patients with severe cholangitis and organ complications require careful monitoring in the Intensive Care Unit (ICU) and effective resuscitation (1). Early biliary decompression is critical in controlling sepsis, and there are numerous methods available, including ERCP with stent insertion, PTBD, ENBD percutaneous cholecystostomy, and open drainage (4). To provide a case illustration, we present a patient who suffered from severe cholangitis and underwent three biliary drainages, including ERCP, PTBD, and percutaneous cholecystostomy, for effective sepsis control.

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Case Report

A 61-year-old woman named Madam H, who has underlying comorbidity diabetes mellitus type 2, hypertension, dyslipidemia, and cholelithiasis, went to HUKM's emergency department with right hypochondriac pain that lasted for a day. She did not experience any fever, tea-colored urine, or pale stool. During the examination, her blood pressure was normotensive at 141/77 mmHg, but her heart rate was tachycardic at 103 bpm. She had a respiratory rate of 18 breaths/min, a

temperature of 36.8°C, and an SPO2 of 99% under room air. Her abdomen revealed tenderness at the right hypochondriac region, yet there was no Murphy's sign, and no evidence of peritonism was found.

After conducting blood tests, it showed that her total bilirubin was elevated at 103, and her liver function test (LFT) was deranged with ALT 201, ALP 312, and AST 203. Other blood parameters were within the normal range. Urgent ultrasonography of the hepatobiliary system was done, which showed a thickened gallbladder wall with lithiasis and a dilated common bile duct (CBD) of 0.8 cm. However, no intraductal lesion or calculus was seen. Diagnosis of mild cholangitis was made. Madam H was admitted to the general ward and given intravenous antibiotics (IV Augmentin 1.2 g TDS).

After two hours of being admitted to the general ward, the patient experienced a temperature spike of 38.5°C and shortness of breath with a respiratory rate of 33 breaths per minute. She required oxygen supplementation through a venturi mask set to 60% to maintain an SPO2 level above 95%. Upon examination of her lungs, bilateral crepitation was detected. An arterial blood gas test revealed type 1 respiratory failure with a pH of 7.43, a PCO2 level of 32, a PO2 level of 73, an HCO3 level of 22.5, and a BE of -3.2. A repeated FBC showed an elevated TWBC of 15.2 and thrombocytopenia with a platelet count of 80. Her LFT was increasing in trends, and the coagulation profile noted a prolonged INR of 1.53. Chest radiography revealed bilateral haziness. As a result, non-invasive ventilation (NIV)-BIPAP was used for oxygen support, and she was diagnosed with severe (Grade III) ascending cholangitis due to respiratory and hematological involvement. Her IV antibiotic was escalated from IV Augmentin to IV Tazocin and fresh frozen plasma (FFP) transfusion was given to correct coagulopathy. Blood culture and sensitivity showed a gram-negative rod.

The patient's condition continued to worsen, and she became more tachypneic despite being on NIV. She was intubated and ventilated to prevent respiratory collapse and resuscitated. An urgent endoscopic retrograde cholangiopancreatography (ERCP) was performed, but CBD cannulation was unsuccessful due to the edematous ampulla of Vater. As a result, the ERCP was abandoned. Following the procedure, she remained persistently hypotensive despite fluid resuscitation. Hence, an intravenous infusion of noradrenaline was started to maintain a mean atrial pressure (MAP) above 65 mmHg. She was then transferred to the intensive care unit (ICU) for close monitoring and. Her condition progressed from mild to severe ascending cholangitis. Since the ERCP failed, percutaneous transhepatic biliary drainage (PTBD) was inserted.

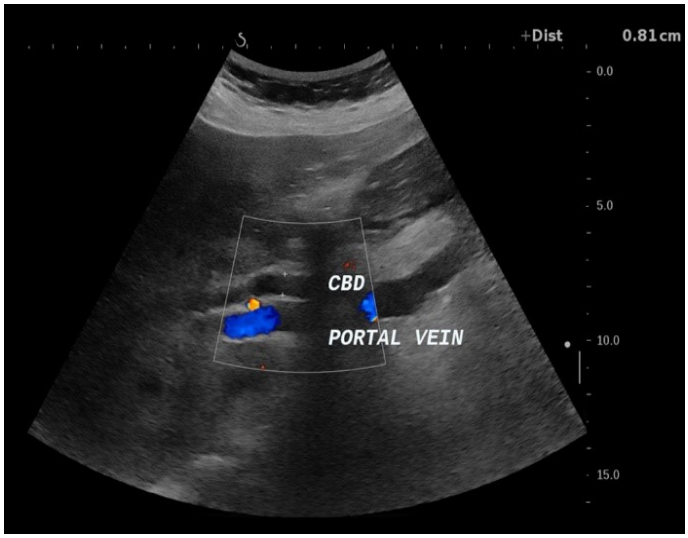

Figure 1. The ultrasonography of the hepatobiliary system reveals a dilated CBD measuring 0.81 cm. This typically indicates an obstructed biliary system, which is often caused by a CBD stone or tumor. However, the study did not find any intraductal lesion or calculus. As a result, urgent ERCP is necessary for both diagnostic and therapeutic purposes

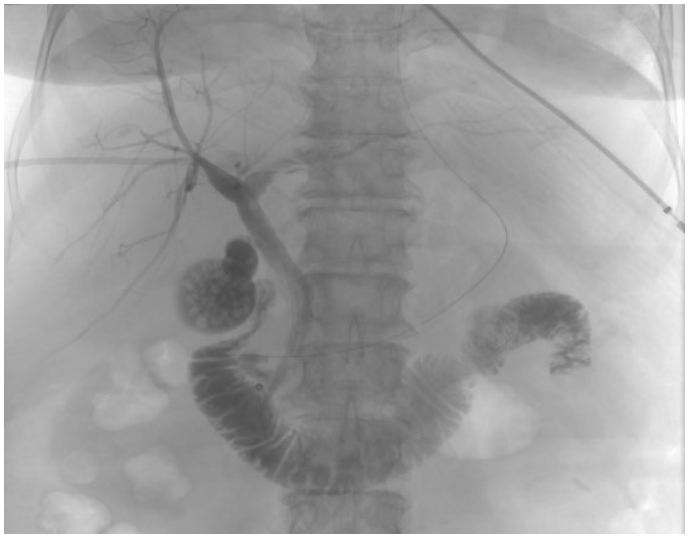

Figure 2. Cholangiogram was performed while inserting a PTBD, which revealed a dilated CBD with abrupt termination at distal CBD/ampulla junction. No filling defect at CBD is seen. Peripheral and main intrahepatic ducts are not dilated. Multiple gallbladder calculi are noted and he tip of the PTBD is located within duodenum

After examining the cholangiogram images of PTBD, a percutaneous cholecystostomy was performed in consultation with the general surgeon. The procedure successfully drained purulent bile. The blood culture and sensitivity test showed the growth of Klebsiella Sp. Based on the blood culture's sensitivity; the antibiotic was changed to IV Unasyn 3 g TDS. The patient's respiratory function improved gradually, and she required low ventilation settings. Her septic parameters and LFT also improved, and she no longer needed inotropic support. The patient will undergo early ERCP and cholangiogram prior to definitive surgery.

Discussion

According to the Sepsis Surviving campaign in 2021, sepsis is a life-threatening dysfunction of the organs caused by an unregulated response to infection. Septic shock, on the other hand, is defined as sepsis with persistent hypotension requiring inotropic support despite adequate fluid resuscitation. Septic shock is also defined by the need for a vasopressor to maintain a patient's mean arterial pressure (MAP) $\geq$ 65 mmHg and serum lactate level $\geq$ 2 mmol/L (1; 5). Since the first consensus definition of sepsis (Sepsis-1) in 1991, the number of cases of sepsis and septic shock has steadily increased, reaching about 49 million cases of sepsis and 11 million sepsis-related deaths worldwide in 2017 (6). Sepsis kills between one in three and one in six of those it affects (1).

Acute cholangitis is a bacterial infection of the hepatobiliary system. It occurs when biliary stenosis whether partial or complete obstruction present in the bile duct or hepatic ducts. The obstruction can be caused by various benign causes (such as bile duct stones, stricture, or occlusion of a stent) or the presence of a tumor, resulting in cholestasis and biliary infection. This biliary stenosis or blockage elevates pressure in the biliary system and flushed the microorganisms or endotoxins from the infected bile into the systemic circulation, inducing a systemic inflammatory response (3). In other postulation, acute bacterial cholangitis or widely known as ascending cholangitis comes from the migration of bacteria from the duodenum into the common bile duct. But, rarely, translocation of bacteria from the portal vein into the bile duct can also occur (2; 3).

It is important to know how to diagnose and grade acute cholangitis to properly stratify the patient, and whether the case can be managed in the general ward or need urgent intervention and monitoring in the critical intensive care unit (ICU). Previously, acute cholangitis has been diagnosed based on Charcot's triad. Studies have shown that Charcot's triad has high specificity

in diagnosing acute cholangitis but has a low sensitivity of around 26% (3). The lack of evidence in this field has prompted specialists to establish a consensus. The first guideline was established in 2007 and the recent revised guideline was in 2018 namely Tokyo Guideline 2018 (TG18) for diagnostic criteria and severity grading of acute cholangitis (3).

The diagnostic criteria for acute cholangitis are based on clinical signs and symptoms, routine blood tests, and diagnostic imaging. While the severity grading is divided into Grade I (Mild), II (Moderate), and III (Severe) acute cholangitis. The severity grading criteria for acute cholangitis are important for predicting prognosis and determining a treatment strategy, especially identifying patients that require early biliary drainage (3). Table 1 in the APPENDIX section shows the TG18/TG13 diagnostic criteria for acute cholangitis while Table 2 shows the severity grading of acute cholangitis (3).

Sepsis caused by acute cholangitis, particularly in moderate and severe acute cholangitis must be treated promptly to prevent septic shock and multiorgan dysfunctions as a patient can deteriorate rapidly. Even with modern treatment, the mortality of sepsis secondary to acute cholangitis can be up to 27% (3). Initial fluids resuscitation and antibiotic must be administrated as per recommendation by Sepsis Surviving Campaign 2021 (1). For sepsis control, urgent biliary decompression must be arranged immediately once the patient is stable after adequate resuscitation (7).

In terms of biliary decompression and drainage, it can be divided into open or endoscopic drainage and internal and external drainage. The most commonly practiced endoscopic drainage is endoscopic retrograde cholangiopancreatography (ERCP). Via ERCP, a stent can be inserted for internal drainage to decompress the biliary system. A Cholangiogram and removal of stone will be performed later on once the patient is out of sepsis and more stable (4).

Those patients who cannot undergo endoscopic drainage will be subjected to external drainage. The widely known procedures for external drainage are endoscopic nasobiliary drainage (ENBD) and percutaneous transhepatic biliary drainage (PTBD). ENBD has advantages where no additional sphincterotomy is required, clogging in the tube (external drain) can be washed out and bile cultures can be done. However, because of the patient's discomfort from the transnasal tube placement, self-extraction and dislocation of the tube are likely to occur, especially in elderly patients. Loss of electrolytes and fluid as well as collapse of tubes by twisting, may also occur (4). For PTBD, it is inserted under ultrasound guided by an interventional radiologist and as per principle. However, PTBD may cause serious complications including intraperitoneal hemorrhage, biliary peritonitis, and a long hospital stay. ERCP and PTBD are also considered difficult procedures as it needs experienced hands to perform the procedure. In ERCP and PTBD, the failure rates are up to 11% and 19% respectively (4).

Percutaneous cholecystostomy is another method for external biliary drainage. It is commonly performed in treating acute cholecystitis. Very few studies explain the role of percutaneous cholecystostomy in the management of acute cholangitis (7). It is applied in treating acute cholangitis, particularly for patients who are critical and unstable for neither endoscopic or PTBD and those who had failed endoscopic drainage. The procedure itself is straightforward. The operator will aim at the distended gallbladder that easily be seen on ultrasound. It is amenable to puncture even if the patient is less cooperative. Therefore, it can be performed in a single attempt of puncture and the procedure can be completed in less than 10 minutes if it is performed by an experienced operator/radiologist (7).

Percutaneous cholecystostomy can also be performed at the bedside in the ward or ICU with a portable ultrasound machine. It can help to reduce the risk of transferring unstable patients to the endoscopy or interventional radiology suite. In addition, the success rate for percutaneous cholecystostomy is almost 100% (7). However, despite the risk and benefits of each external and internal drainage method, previous RCTs have shown there is no difference between external drainage and stent placement (internal drainage) for treating acute cholangitis (4). The choice of drainage is based on the patient's general condition and the availability of endoscopic/PTBD facilities and expertise in each hospital.

For the open technique, T-Tube insertion is commonly performed. It is indicated for patients who

cannot undergo such noninvasive procedures due to anatomical and structural reasons, such as patients who had undergone Roux-en-Y choledochojejunostomy procedures. In open drainage, the goal is similar which is to decompress the biliary system. Simple procedures such as T-tube placement without choledocholithotomy should be recommended. This is because long hours of operations should be avoided in such ill patients (3).

Conclusion

Sepsis is a life-threatening organ dysfunction due to infection which has high mortality and morbidity. While acute cholangitis is the most common cause of biliary sepsis which can progress rapidly into septic shock and fatal. Diagnosing and grading acute cholangitis is important to stratified patients and helps in the next treatment plans. Early biliary drainage for decompression is needed for sepsis control in obstructed biliary sepsis. Biliary decompression can be achieved by ERCP and stenting, ENBD, PTBD, or open drainage. Percutaneous cholecystostomy is also another method of biliary drainage in acute cholangitis. The choice of drainage must be chosen properly based on the patient's general condition and the availability of the facility in each hospital.

Conflict Of Interest

All authors declare no conflict of interest of any kind.

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Appendix

Diagnostic Criteria and Severity Grading of Acute Cholangitis according to Tokyo Guideline 2018.

Table 1. TG18/TG13 diagnostic criteria for acute cholangitis

A. Systemic inflammation			
A-1. Fever and/or shaking chills			
A-2. Laboratory data: evidence of inflammatory response			
B. Cholestasis			
B-1. Jaundice			
B-2. Laboratory data: abnormal liver function tests			
C. Imaging			
C-1. Biliary dilatation			
C-2. Evidence of the etiology on imaging (stricture, stone, stent etc.)			
Suspected diagnosis: one item in A + one item in either B or C			
Definite diagnosis: one item in A, one item in B and one item in C			
Note:			
A-2: Abnormal white blood cell counts, increase of serum C-reactive protein levels, and other changes indicating inflammation			
B-2: Increased serum ALP, r-GTP (GGT), AST, and ALT levels Other factors which are helpful in diagnosis of acute cholangitis include abdominal pain (right upper quadrant or upper abdominal) and a history of biliary disease such as gallstones, previous biliary procedures, and placement of a biliary stent. In acute hepatitis, marked systematic inflammatory response is observed infrequently. Virological and serological tests are required when differential diagnosis is difficult.			
Thresholds:			
A-1	Fever		B-T >38°C
A-2	Evidence of inflammatory response	WBC count (× 1.000/μL)	<4 or >10 ≥1
		CRP(mg/dL)	
B-1	Jaundice		T-Bil ≥2 (mg/dL)
B-2	Abnormal liver function tests	ALP (IU)	>1.5× STD
		GTP (IU)	>1.5× STD
		AST (IU)	>1.5× STD
		ALT (IU)	>1.5× STD
Cited from Kiriyama et al.[4]			
ALP alkaline phosphatase, ALT alanine aminotransferase, AST aspartate aminotransferase, CRP C-reactive protein, r-GTP (GGT) r glutamyltransferase, WBC white blood cell			
STD: upper limit of normal value			

Table 2. TG18/TGI3 severity assessment criteria for acute cholangitis [4]

Grade III (severe) acute cholangitis "Grade III" acute cholangitis is defined as acute cholangitis that is associated with the onset of dysfunction at least in any one of the following organs/systems: 1. Cardiovascular dysfunction: hypotension requiring dopamine ≥5 μg/kg per min, or any dose of norepinephrine 2. Neurological dysfunction: disturbance of consciousness 3. Respiratory dysfunction: PaO2 /FiO2, ratio <300 4. Renal dysfunction: oliguria, serum creatinine >2.0 mg/dl 5. Hepatie dysfunction: PT-INR >1.5 6. Hematological dystunction: platelet count <100,000/mm^3 Grade II (moderate) acute cholangitis "Grade II" acute cholangitis is associated with any two of the following conditions: 1. Abnormal WBC count (>12,000/mm^3, <4,000/mm^3) 2. High fever (≥39°C) 3. Age (≥75 years old) 4. Hyperbilirubinemia (total bilirubin ≥5 mg/dl) 5. Hypoalbuminemia (<STD"x0.7) Grade I (mild) acute cholangitis ""Grade I" acute cholangitis does not meet the criteria of "Grade III (severe)" or ""Grade II (moderate)" acute cholangitis at initial diagnosis.
Early diagnosis, early biliary drainage and/or treatment for etiology, and antimicrobial administration are fundamental treatment for acute cholangitis classified not only "Grade III (severe)" and "Grade II (moderate)" but also "Grade I (mild)". Therefore, it is recommended that patients with acute cholangitis who do not respond to the initial medical treatment (general supportive care and antimicrobial therapy) undergo early biliary drainage or treatment for etiology (see flowchart). Cited from Kiriyama et al. [4] STD: lower limit of normal value