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Case Report

Percutaneous Transhepatic Gallbladder Drainage for Acute Cholecystitis During Chemotherapy: Case Series

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Abstract: Clinicians may have trouble treating acute cholecystitis in patients undergoing chemotherapy. This study aimed to review the feasibility of continuing chemotherapy while a biliary tube is in place and report our experience. We retrospectively examined the records of 17 patients who underwent percutaneous transhepatic gallbladder drainage (PTGBD) for acute cholecystitis. The cohort comprised nine cases of gastrointestinal cancer and eight other malignancies. Overall, chemotherapy was resumed in 12 cases after PTGBD. These patients were divided into three groups based on the circumstances under which chemotherapy was resumed. Chemotherapy was performed with the drain in place in seven patients (14.33±6.94 days until the start of chemotherapy after drainage, group A), after cholecystectomy in three (84±56 days, group B), and after removing the drainage tube (56 days, group C) in two patients. Early administration of chemotherapy was only possible in group A. At times, clinicians are required to make complicated judgments regarding acute cholecystitis treatment that cannot be done by relying on guidelines alone. With strict control, chemotherapy can be safely resumed, even with a drainage tube in place, and PTGBD can be carefully considered for these patients. These groups were determined retrospectively based on the course of treatment.

Keywords: Acute Cholecystitis; Case Series; Chemotherapy; Gallbladder; Drainage; Cholecystectomy.

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1. Introduction

Acute cholecystitis with neutropenia has a poor prognosis, with a mortality rate of 26.7% [1]. It is associated with increased postoperative mortality and complicating treatment. We report our experience in a small number of oncology patients with cholecystitis treated with percutaneous transhepatic gallbladder drainage (PTGBD). Adverse events, such as pancytopenia, may occur during chemotherapy [2], and deciding on the treatment course for acute cholecystitis during chemotherapy can be challenging.

There is limited evidence or guidance on whether and when to resume chemotherapy following PTGBD. Therefore, this study aimed to review the feasibility of continuing chemotherapy while a biliary tube is in place. This report follows the PROCESS Guideline [3], recognizing its descriptive nature and the inherent limitations of a small, retrospective case series without comparative controls.

2. Case Report

2.1 Methods

We reviewed the records of 17 patients who developed acute cholecystitis and underwent PTGBD while being admitted to our hospital for treatment of malignant disease between January 2003 and December 2020. In this retrospective study, the diagnosis and severity of acute cholecystitis were assessed using patient records and the Tokyo Guidelines 2018 (TG18) [4]. During the study period, it was hospital policy to first perform PTGBD, without exception, for patients who developed acute cholecystitis while being treated for malignant diseases. Percutaneous biliary drainage was performed by a dedicated drainage physician at the Department of Hepatobiliary and Pancreatic Surgery.

The same physician oversaw subsequent tube management during hospitalization until the removal of the tube after discharge. For approximately one week after drain tube insertion, follow-up consultations and radiographs were performed to check for tube deviation or obstruction. If necessary, the tube was flushed with saline solution and repositioned under fluoroscopic guidance. Because of the risk of tube deviation until fistula formation, patients were followed closely until discharged to detect tube complications as early as possible. The attending physicians from the Department of Hepatobiliary and Pancreatic Surgery discussed the cases and reached a consensus on the appropriate timing for chemotherapy resumption since there were no established criteria for chemotherapy resumption; however, it was essential that the patient's oncologist and hepatobiliary and pancreatic surgeon agreed.

Our decision-making process included multidisciplinary evaluation based on ECOG PS, comorbidities, infection control, and overall clinical condition. The primary outcome was successful drain maintenance, which was defined as PTGBD without major adverse events. Additional factors included patient age and sex, tube size, and length of the drain. We evaluated adverse events using the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 [5] and performance status using the Eastern Cooperative Oncology Group (ECOG) performance status (PS) scale [6]. Descriptive statistics were calculated. All values are presented as mean ± standard deviation or number (%), unless otherwise stated. No comparative statistical analysis was carried out. This grouping was constructed post hoc and not based on pre-specified criteria. No comparative statistical analysis was conducted, and descriptive statistics were used.

2.2 Case Report Description

The age of 17 patients in our study cohort ranged from 47 to 85 years. The malignancies being treated included four cases of gastric cancer, four of colorectal cancer, two of esophageal cancer, two of lung cancer, three of malignant lymphoma, one of osteosarcoma, and one of tongue cancer. Cholecystitis severity was classified as severe (three cases), moderate (eleven cases), or mild (three cases) (Table 1). During the period in which the drainage tube was indwelling, grade 2 (or higher) adverse events due to chemotherapy were observed in two patients. Grade 4 leukopenia was reported in one patient with lung cancer, and grade 4 anorexia was reported in one patient with esophageal cancer.

No adverse events were observed during tube placement in patients with malignant lymphoma. None of these adverse events required treatment and all outcomes of acute cholecystitis were curative. Five patients were transferred to other institutions to receive supportive care following the cure of cholecystitis, but chemotherapy was not resumed because of a decline in PS due to malignancy progression, among other reasons (Figure 1).

Five patients were transferred to receive supportive care following cholecystitis cure but underwent no chemotherapy because of a decline in performance status due to malignancy progression, among other reasons. Chemotherapy was resumed in 12 patients and these patients were divided into groups based on the circumstance under which chemotherapy was resumed. Chemotherapy was administered with the drain in situ in

seven patients (14.33±6.94 days to chemotherapy after drainage, group A). Three patients underwent cholecystectomy after drainage followed by chemotherapy (84±56 days to chemotherapy after drainage, group B), and two started chemotherapy after drainage tube removal (56±0.00 days to chemotherapy after drainage, group C). The disease breakdown and time of chemotherapy administration are shown in Table 2. Early resumption of chemotherapy was only possible in group A.

The malignancies in group B were hematological, comprising two malignant lymphomas and one osteosarcoma, which are generally associated with more adverse events than gastrointestinal malignancies. Both patients in group C had severe cases of cholecystitis, which were cured, but they experienced intensive care unit-acquired weakness (ICU-AW). Due to this, a long period was needed before reopening, and post-drainage chemotherapy could only be initiated after 56 days. Grouping was based on the actual clinical course and underlying disease characteristics. Group B typically involved hematologic malignancies requiring more intensive monitoring, whereas group C patients developed ICU-acquired weakness, delaying chemotherapy resumption.

Table 1. Severity of cholecystitis, tube removal post percutaneous transhepatic gallbladder drainage, chemotherapy regimen, and patient performance.

Age (years)	Malignancy	Cholecystitis severity	Regimen	Removal of the tube post PTGBD	Period until chemotherapy resumption/initiation	Performance status at chemotherapy initiation	Adverse event during tube placement
65	Colon cancer	Moderate	UFT→none	No removal	None	Not recorded	-
75	Gastric cancer	Moderate	TS-1→none	No removal	None	Not recorded	-
79	Gastric cancer	Moderate	None	No removal	None	Not recorded	-
67	Colon cancer	Severe	FOLFOX	Removal	8 weeks	1	-
80	Gastric cancer	Severe	TS-1→5'-DFUR	Removal	8 weeks	1	-
70	Gastric cancer	Moderate	TS-1→CDDP +CPT11	No removal	2 weeks	1	-
71	Rectal cancer	Severe	TS-1＋CPT11	Removal	2 weeks	1	-
67	Esophageal cancer	Moderate	CDDP＋5FU	Postoperative removal	2 days	1	Anorexia: Grade 4
47	Osteosarcoma	Moderate	IFM	Postoperative removal	4 weeks	0	-
68	Colon cancer	Moderate	UFT/UZEL	Postoperative removal	2 weeks	1	-
62	Lung cancer	Mild	Durvalumab	No removal	3 weeks	1	-
60	Malignant lymphoma	Moderate	R-CHACE	Postoperative removal	20 weeks	0	-
85	Tongue cancer	Moderate	None	Postoperative removal	None	Not recorded	-
59	Esophageal cancer	Mild	TPF→none	Postoperative removal	None	Not recorded	-
80	Malignant lymphoma	Mild	R-CHOP→VP-16	Postoperative removal	12 weeks	1	-

78	Malignant lymphoma	Moderate	R-CHOP	Postoperative removal	3 weeks	1	-
60	Lung cancer	Moderate	CBDCA＋PEM	No removal	3 weeks	0	Leukopenia: Grade 4

UFT: tegafur–uracil; TS-1: tegafur, gimeracil, oteracil potassium; FOLFOX: folinic acid, fluorouracil, oxaliplatin; 5'-DFUR: doxifluridine; CDPP: cisplatin; CPT11: irinotecan; IFM: ifosfamide; UZEL: calcium folinate; R-CHACE: rituximab, cyclophosphamide, cytarabine, etoposide, dexamethasone; TPF: docetaxel hydrate, cisplatin, 5-fluorouracil; VP-16: etoposide; R-CHOP: rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine; CBDCA＋PEM: carboplatin, pemetrexed sodium hydrate; PTGBD: percutaneous transhepatic gallbladder drainage.

Figure 1. Post-drainage findings.

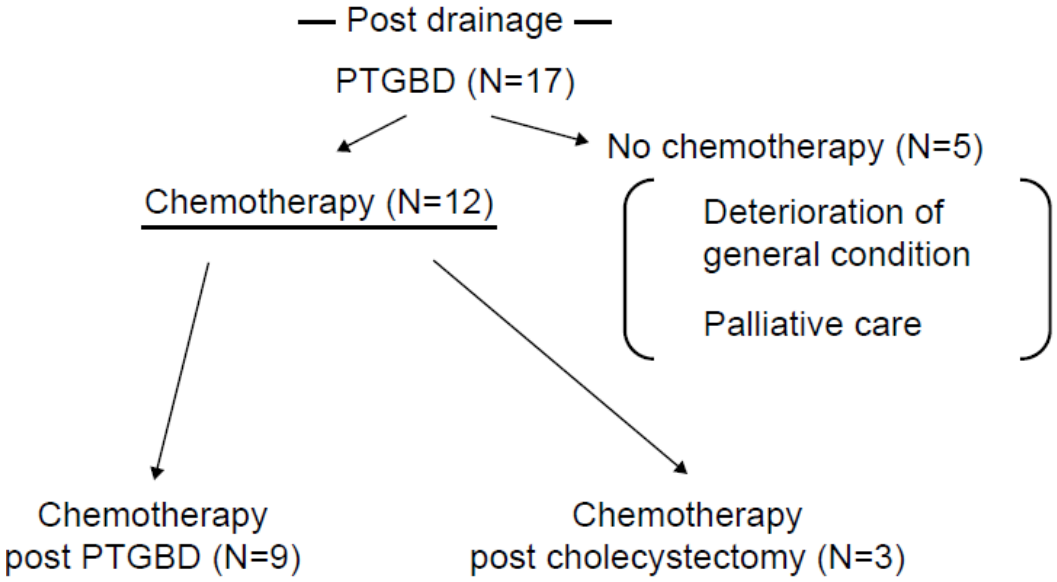

Table 2. Cancer type and period until chemotherapy resumption.

Group	A	B	C
Number of patients	7	3	2
Chemotherapy initiated after drainage (days) (mean ± standard deviation)	14.33±6.94	84±56	56±00
Type of cancer	Esophageal: 1 Gastric: 1 Rectal: 1 Colon: 1 Lung: 2 Malignant lymphoma: 1	Osteosarcoma: 1 Malignant lymphoma: 2	Colon: 1 Gastric: 1

A representative case for each group is presented below:

Group A, Case 1: A 67-year-old man with a preoperative diagnosis of Stage IVa esophageal cancer underwent right thoracotomy, subtotal esophagectomy, and gastric

tube reconstruction. The postoperative pathological diagnosis was T4N4M0 Stage IVb. A radical chemoradiation therapy regimen of 50 Gy + Cisplatin (CDDP) 10 mg + Fluorouracil (5FU) 500 mg was scheduled for 4 weeks after surgery. On postoperative day 32, before chemotherapy could be initiated, the patient developed moderate-acute cholecystitis, and PTGBD was performed on the same day. After two days of drainage, good progress was observed, and chemotherapy was initiated. After six weeks of chemotherapy, the patient underwent laparotomy cholecystectomy, and the drainage tube was simultaneously removed. During the chemotherapy period, a dedicated drainage physician closely monitored the patient to ensure early detection of any tube obstruction or deviation; however, the patient showed no tube-related complications that interrupted chemotherapy. After the appearance of lung metastases, chemotherapy with paclitaxel 80 mg + CDDP 10 mg + 5FU 500 mg was initiated eight weeks after open cholecystectomy.

Group B, Case 2: A 60-year-old man with gastric malignant lymphoma was treated with rituximab, cyclophosphamide, doxorubicin hydrochloride, and vincristine (R-CHOP), and achieved remission. However, mediastinal recurrence occurred after two years and the patient was subsequently treated with rituximab, cyclophosphamide, cytarabine, etoposide, and dexamethasone (R-CHASE), and achieved a partial response. The patient was admitted to the hospital for autologous peripheral blood stem cell transplantation, which required pre-transplantation treatment with high-dose chemotherapy. Before treatment could commence, the patient developed acute cholecystitis. We proposed PTGBD and initiation of chemotherapy. After discussion with the Hematology Department, they decided against treatment with the PTGBD catheter in situ. It was therefore decided to perform cholecystectomy, remove the drainage tube at the time of surgery, and initiate chemotherapy thereafter. The patient progressed without complications from cholecystectomy, including wound infection; however, it was decided that treatment should only be initiated when the surgical wound was completely healed. Chemotherapy was subsequently resumed 20 weeks after PTGBD.

Group C, Case 3: An 80-year-old man presented with lung metastasis and intra-abdominal lymph node recurrence three years after surgery for Stage IIIB gastric cancer, and was being treated with tegafur, gimeracil, and oteracil potassium. PTGBD and liver abscess drainage were performed to treat severe cholecystitis. It was decided to not perform cholecystectomy because of a history of ischemic heart disease and ICU-AW. The cholecystitis was resolved, and the tube was removed on day 16 after drainage. After the patient's general condition improved, chemotherapy was resumed eight weeks after drainage.

Patient QOL and follow-up: Although formal quality-of-life assessments were not performed, some patients required extended hospitalization to ensure tube maintenance and safety. While no complaints lead to early drain removal or therapy interruption, the presence of an external drain may impact on patient comfort, mobility, and infection risk, and therefore require careful monitoring.

3. Discussion and Conclusion

In this study, we reviewed the feasibility of continuing chemotherapy while a biliary tube is in place. We believe that, in some cases, chemotherapy is possible even with a biliary drain in place. We also found that the type of malignancy was a big factor in feasibility. At our institution, PTGBD was performed in all patients with acute cholecystitis undergoing chemotherapy, and we reported on the course of these PTGBD-treated cases. Tube management by the Hepatobiliary and Pancreatic Surgery Department proved to be important and chemotherapy could safely be performed in seven of twelve patients with the tube in situ. Since patients in need of chemotherapy with cholecystitis is a subject that is not defined in the current guidelines, we have reported a small number of cases. The treatment strategy for acute cholecystitis has been revised and re-established since the original publication of the guidelines [4,7]. The revised "Tokyo Guidelines 2018 (TG18): flowchart for the management of acute cholecystitis" includes a major change relating to

early surgery. In the TG13, early surgery for severe cases is not recommended; however, in the TG18, early surgery is recommended for patients who respond well to initial treatment and administration of antihypertensive drugs and are at risk for surgery [4].

In the TG18, both the severity of acute cholecystitis and underlying diseases are considered, and the guidelines were adapted to select the treatment method according to the surgical risk. This change allows for better clinical decisions while following the guidelines. Under these guidelines, clinicians utilize the Charlson Comorbidity Index (CCI) [8], the American Society of Anesthesiologists Physical Status Classification System, and other predictors to assess the viability of surgery. The CCI determines a patient's surgical risk, and a higher total score represents a higher predicted mortality rate. The CCI includes cancer status in addition to systemic diseases, such as myocardial infarction, congestive heart failure, cerebrovascular disease, and dementia. However, when considering pathological conditions, with a focus on cancer treatment, the carcinomatous state varies from case to case, and complex decisions, which cannot be made based on guidelines alone, may be required.

In acute cholecystitis management in the carcinomatous state, Santos et al. reported that PTGBD was useful until standby surgery could be performed [9]. However, while Santos et al. mention the indications for surgery and drainage, they do not discuss the subsequent resumption of chemotherapy. Other reports on cholecystitis treatment are similar, with no mention of subsequent resumption of chemotherapy. Although the World Society of Emergency Surgery, Surgical Infection Society Europe, World Surgical Infection Society, American Association for the Surgery of Trauma, and Global Alliance for Infection in Surgery guidelines provide recommendations for the treatment strategy for cholecystitis in immunocompromised patients [10], recommendations for chemotherapy resumption timing have not been discussed.

In practice, the prognosis and adverse events associated with chemotherapy vary widely and must be considered on a case-by-case basis. Two of the cases presented here are particularly contrasting. The first case included a relatively adverse chemotherapy regimen for gastrointestinal surgery; however, chemotherapy was initiated on the second day after drainage with the tube in place. Under strict tube management, the chemotherapy schedule was only slightly altered. Conversely, the second patient was scheduled to receive high-dose chemotherapy and other pre-transplant procedures for autologous peripheral blood stem cell transplantation. However, the clinicians opted for cholecystectomy and chemotherapy initiation only thereafter. According to Santos et al., oncologists often delay cancer treatments until cholecystectomy is performed because strict treatment protocols advise against the presence of abdominal drains during treatment [10].

Drain management during chemotherapy for biliary or pancreatic cancer is especially helpful when considering the resumption of chemotherapy with a PTGBD tube in place. The treatment of malignancies in the biliopancreatic region often requires biliary drainage. However, even though biliary drainage is widely used in the daily practice of chemotherapy for biliary and pancreatic cancers and biliary tract cancer guidelines describe preoperative biliary drainage in detail, they do not make specific recommendations for drainage management during chemotherapy. We considered that chemotherapy could be administered immediately following cholecystitis treatment if drainage management was performed properly. Biliary drainage is commonly performed following gastrointestinal surgery. In addition, chemotherapy for gastrointestinal malignancies generally involves relatively fewer adverse events than chemotherapy for hematological and other malignancies. This may explain why chemotherapy resumption during drainage was viable for some patients. Conversely, in the hematological cases presented here, indwelling drainage tube placement was reinitiated in only one of the three cases of malignant lymphoma under strict tube management. The presence of an abdominal drain may hinder chemotherapy resumption; therefore, it was considered difficult to perform PTGBD in all the drainage cases, except in patients with gastrointestinal disease.

At the time when some of these cases were reported, the treatment policy was to promptly perform PTGBD, even in mild cases of acute cholecystitis, if antimicrobial agents were not effective. Thus, PTGBD was performed in three mild cases. The current policy instructs that such patients should be treated with early surgery if antimicrobial therapy is ineffective. In one case, the period from drainage to chemotherapy resumption was delayed and lasted 20 weeks. In retrospect, early surgery should have been considered, and the same consideration will be applied in the future.

Alternatively, endoscopic transpapillary gallbladder drainage (ETGBD) and endoscopic ultrasound-guided gallbladder drainage (EUS-GBD) have been used as drainage techniques for acute cholecystitis. Hatanaka et al. reported the safety and usefulness of EUS-GBD in patients with carcinomas who were not eligible for early cholecystectomy [11]. Endoscopic techniques such as ETGBD or EUS-GBD were not adopted during the study period due to a lack of institutional expertise and availability. However, these should be considered in future protocols, particularly for high-risk surgical patients. Therefore, ETGBD or EUS-GBD can be considered when it can be performed by skilled endoscopists at high-volume institutes [12,13]. In retrospect, ETGBD or EUS-GBD could have been considered in some of our reported cases, and this consideration will be applied in future with possible modifications to our institutional protocols. EUS-GBD is also expected to allow early improvement in ICU-AW, which was a complication for patients in group C, as the tube is situated internally and does not interfere with early rehabilitation in the ICU, unlike in the case of PTGBD.

Finally, without a treatment group, we are limited to historical comparisons to evaluate our small number of patient records. Given the unique indication of patients undergoing chemotherapy with the PTGBD drain in situ (group A), a prospective trial is unlikely. However, a multicenter retrospective analysis with demographic- and pathology-matched controls would significantly improve the interpretability and reliability of our findings. These techniques were not widely adopted during the study period due to institutional constraints, but future revisions to our protocol will actively consider their use in eligible cases. Finally, this study has several limitations: small sample size, retrospective design, lack of a comparison group, and heterogeneity of malignancy types and chemotherapy regimens. Despite these, our findings provide initial evidence that may inform clinical judgment in an area with minimal existing data. A prospective or multicenter matched retrospective study would enhance external validity and help define clearer criteria for safe chemotherapy resumption in this context.

In conclusion, following acute cholecystitis, it is possible that, in some patients, chemotherapy can be safely initiated or resumed with the PTGBD tube in place, provided strict drainage management is performed with a multidisciplinary approach including oncologists and surgeons. Appropriate management, including PTGBD, is required if the onset of acute cholecystitis occurs during cancer treatment. In future, we intend to actively consider the use of PTGBD in patients with cancer who are not eligible for early cholecystectomy as an effective means to improve quality of life.

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