

# A rare cause of gallbladder perforation: Burkitt's lymphoma

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## ABSTRACT

Although the perforation of gallbladder rarely occurs, it is a high-risk and life-threatening condition. High rates of mortality and morbidity are associated with late diagnosis. Burkitt's lymphoma is a disease, which starts in B-cells and develops with leukemia and extranodal involvement. Involvement of gallbladder wall is a very rare location of extranodal lymphomas. In this case, a 68-year-old woman with severe pain in the left arm referred to our outpatients' clinic where anti-HCV (+), leukocytosis, elevated sedimentation rate, and thrombocytopenia were found in her initial tests. On the basis of these findings, further tests were performed and she was diagnosed with Burkitt's lymphoma. She had acute abdomen and gallbladder perforation was detected by radiologic study. Urgent laparotomy was performed and she subsequently underwent cholecystectomy and drain insertion. Postoperative septic shock developed and she died due to multiple organ dysfunction syndrome. The determined diagnosis was described as gallbladder wall perforation associated with Burkitt's lymphoma infiltration in the pathology report. It is very important for the clinicians to take into the consideration that a rare cause of gallbladder perforation is Burkitt's lymphoma and it has an aggressive postoperative clinical course.

**Keywords:** Gallbladder perforation, Burkitt's lymphoma

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**G**allbladder perforation is a rare but life-threatening condition. Acute cholecystitis may be seen in 2-15% of the patients and it is usually observed with gallbladder stones [1, 2]. Although gallbladder perforation has been uncommonly seen, mortality is high with a rate of 12-42% [1, 3, 4]. Thus, it is very important to establish an early diagnosis and immediate medical treatment.

The associating illnesses in the patients with gallbladder stone disease predispose the development of gallbladder perforation. In immunocompromised patients, when the cholecystitis cannot be contained the disease may progress causing perforation. Besides, the diseases involve the gallbladder wall may also cause

perforation. In this case report, we aim to scrutinize the gallbladder perforation developed secondary to Burkitt's lymphoma which both impairing the immune system and infiltrating the gallbladder wall and also to share this case illustrating a sample that is not described in the literature so far.

## CASE PRESENTATION

A 68-year-old woman was admitted to our orthopedic clinic with the complaints of pain in her left arm. Since no fractures has been identified in her initial examination, she was referred to infectious



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diseases department with the pre-diagnosis of liver cirrhosis process based on anti-HCV (+), leukocytosis, elevated sedimentation, and thrombocytopenia findings. Patient was hospitalized for further examinations and treatment. In her anamnesis, she reported appetite loss, night sweats, weight loss, and fever. She had no specific past medical history but hypertension. During her hospitalization, no significant clinical manifestation has been found with the exception of slight hyperemia in the upper inner (superomedial) quadrant of the left breast and edema in the left upper extremity.

Upper extremity venous color doppler Ultrasonography showed thick, heterogeneous, and edematous tissue layer under the skin surface and multiple lymphadenopathies (maximum 25×26 mm in diameter). Furthermore, presence of lymphadenopathies in the left supraclavicular region and edema caused pressure on the left subclavian and axillary arteries have also been detected.

Abdominal ultrasonography showed gallbladder wall thickness of 10 mm and edematous appearance (cholecystitis). Deformation on gallbladder lateral walls was observed and found to be equivocal with respect to gallbladder perforation. Hypoechoic images were observed in the gallbladder, with the largest of which was matching with a 1 mm stone. Abdominal Computed Tomography (CT) showed increased gallbladder distention and wall thickening, and also fluid collection in the pericholecystic area (acute cholecystitis). A collection area of 2.5×2 cm has been detected on the gallbladder lateral walls between the gallbladder and the liver. Poorly defined gallbladder walls have been noted (perforation). There were large numbers of lymph nodes in the paraaortic region none of which regarded as pathological (Figure 1). Thoracic CT showed diffuse thickness on the left thoracic wall and beneath the skin surface of the left breast, and increased density (abscess? or hematoma?).

The patient was administrated with 4×1 gr of ampicillin sulbactam for the cellulitis in her left breast. Hematology consultation was made when the thrombocyte level decreased from 40,000 to 19,000. Since Burkitt's-like cells had been observed in the peripheral smear, the patient was pre-diagnosed with acute lymphocytic leukemia (ALL) or lymphoma. Lymph node excisional biopsy and bone marrow biopsy were planned for the patient. Meanwhile,

general surgery consultation was requested since she manifested acute abdomen clinical table.

After the general surgery consultation; the results were evaluated as follows; her general condition was poor, body temperature was 37.5 °C, (99.5°F), had a positive Murphy's sign, and there was sensitivity in the other quadrants of the abdomen but no muscular defence. As a result of patient's clinical and radiologic evaluation, she was transferred into general surgery clinic for emergency laparotomy with the diagnosis of lymphoma? + ALL? Preoperative fluid resuscitation, antibiotherapy, and thrombocyte replacement were performed. Patient, whose anesthetic risk reported as ASA IV E, underwent an emergency laparotomy. Exploration revealed that gallbladder wall at the liver side was perforated and abscesses formed in the intraparenchymal area. Open cholecystectomy + debridement + drainage processes were applied.

Thrombocyte apheresis and erythrocyte replacement were performed during and after the surgery. In the first preoperative day, general condition of the patient worsened and hemorrhagic exudate leaving the drains and incision lines were observed. The patient had 38.5°C (101.3 °F) fever, oliguria, hypotension, tachycardia, and tachypnea, then she also had septic shock and subsequently multiple organ dysfunction syndrome. The patient not responding to resuscitative interventions died. Morphological and immunohistochemical findings of the case are "Burkitt's lymphoma".



**Figure 1.** Gallbladder perforation area.

## DISCUSSION

Gallbladder perforation is an uncommon but life-threatening condition. Sometimes it may not be differentiated from uncomplicated acute cholecystitis and may result in morbidity and mortality due to delayed diagnosis [1, 2]. While gallbladder perforation rate could be seen as 2-15 % in the patients with acute cholecystitis, this rate was observed between 3.3-5.9% when evaluated along with acute and chronic gallbladder perforations [3-5].

According to Neimer classification, gallbladder perforation divides into three subtypes. Type-1 is called acute free perforation and associated with generalized biliary peritonitis. Type-2 is called subacute pericholecystic abscess and associated with peritonitis. Type-3 is called chronic cholecystoenteric fistulation and associated with fistula [6]. The appearances of these types are different from each other. Type-1 patients are usually immune impaired thus, the disease cannot be localized and consequently lead to free perforation and generalized peritonitis. While Type-2 patients are monitored in subacute care clinics, Type-3 patients develop chronic cholecystitis and it is very difficult to diagnose unless they present with obstructive hepatitis symptoms [2, 3]. In the pathological analysis of this case, it has been considered that; Type-2 perforation was developed due to Burkitt's lymphoma infiltration into gallbladder wall, and also as secondary to immune insufficiency caused by Burkitt's lymphoma and probable bone marrow suppression, disease could not be controlled and the prognosis rapidly progressed into multiple organ dysfunction syndrome.

Gallbladder perforation may occur within the 24 hours after acute cholecystitis, as well it may develop in between a couple of days and weeks [7]. It is not possible to predict in which patient gallbladder perforation will develop [2, 3, 8]. Prognostic risk factors such as older age, male gender, associating illnesses, fever 38°C (100.4 °F), elevated white blood cell (WBC) count may indicate the patients in whom the complications such as gangrene, empyema, emphysematous cholecystitis, and perforation could occur [9, 10].

Some associate systemic diseases such as atherosclerotic heart disease, diabetes among these prognostic risk factors may induce ischemia of the

gallbladder wall, causing to necrosis and perforation [1, 3]. Furthermore, in the medical conditions where immune system is suppressed, the disease may also progress leading to perforation. In this case report, 68 years-old patient's higher age group, Burkitt's lymphoma and hypertension as associating illnesses, fever >37.5°C (99.5°F), WBC of 17.3 10<sup>9</sup>/L are all matching with the literature in terms of the risk factors. It has been thought that these risk factors led to gallbladder perforation.

It is very difficult to preoperatively diagnose gallbladder perforation. Perforation of the gallbladder wall appears as defect on abdominal ultrasonography, furthermore abdominal CT contributed to increasing the accuracy in diagnosis [8]. Once the gallbladder perforation was diagnosed, it is of most importance that an immediate surgical intervention should be performed for diminishing morbidity and mortality [2]. In this case, gallbladder perforation was accurately diagnosed with both abdominal ultrasonography and abdominal CT and immediate laparotomy was performed.

One of the diseases, which cause to immune system impairing, is Burkitt's lymphoma. Burkitt's lymphoma is a disease, which starts in B-cells, aggressively progressing and developing a course with leukemia and extranodal involvement [11]. It has a low incidence of occurring in the adults [12]. Its incidence is 0.3/100.000 in US [13]. Appetite loss, night sweats, weight loss and fever symptoms present in the clinical table of Burkitt's lymphoma. Our patient had also presented appetite loss, night sweats, weight loss and fever at the time of admittance. So BL's stage accepted stage4B because of organ infiltration (gallbladder) and probable bone marrow infiltration (thrombocytopenia).

In the classification, there are three types of Burkitt's lymphoma: endemic, sporadic, and immunodeficiency-associated. While the endemic variant usually observed as tumors of the Jaw, sporadic type seen in the abdomen [14]. In our country Burkitt's lymphoma occurs mainly with abdominal diseases (70%) then with the involvement of orbit and jaw (45%) [15-18]. Although sporadic Burkitt's lymphoma is rarely seen in adults, it has an aggressive prognosis. Involvement of the gastrointestinal system is typical and it occurs most commonly in the ileocecal region, rarely seen in stomach or duodenum primarily.

[19, 20].

Common clinical presentations of Burkitt's lymphoma include intestinal obstruction and intussusception [21]. Liver, spleen, bone marrow, central nervous system; and less commonly skin, eyes, thyroid, bones, breasts and gonads are the regions where extranodal involvement occurs [22]. In literature, Burkitt's lymphoma coexisting in gallbladder and rectum has been reported only for an 11-year-old boy and it was presented as an unusual case [23]. Extranodal site of involvement of Burkitt's

lymphoma was also gallbladder in that case.

Acute phase reactants such as sedimentation rates, C-reactive protein and procalcitonin levels found to be elevated in the biochemical blood analysis and hemogram testings. Expected high levels of lactate dehydrogenase and elevated uric acid levels in most patients with Burkitt's lymphoma were also measured greater than the reference ranges in this case. High levels of tumor markers were measured. Furthermore, it has been thought that the presence of thrombocytopenia in hemogram analysis and post-

**Table 1.** Laboratory results of the patient in admission, pre- and postoperative periods

	Admission	Preoperative	Postoperative
White blood cells (4-10 10 <sup>9</sup> /L)	11.5	17.3	25.1
Hemoglobin (3.5-5 gr/dl)	11.5	13.7	10.3
Hematocrit (34-47 %)	33.6	29.5	41
Platelets (110-300 10 <sup>9</sup> /L)	40.000	53.000	83.000
CRP (0-5 mg/L)	216	-	-
Sedimentation (1-20 mm/h)	70	-	-
Procalcitonin (0-0.046 ng/dl)	0,92	-	-
Anti HCV (0-1 COI)	+	+	+
HCV RNA	Negative	Negative	Negative
Anti-HBs (2-10 IU/L)	< 2	< 2	< 2
Anti HIV (0-1 COI)	Negative	Negative	Negative
HbsAg (0-1 COI)	Negative	Negative	Negative
AST (15-37 IU/L)	98	185	56.5
Urea (15-38.5 mg/dl)	21	40.6	53.9
Creatinine (0.6-1 mg/dl)	1.19	1.99	1.57
Total bilirubin (0.2-1 mg/dl)	1.7	1.8	1.9
Direct bilirubin (0-1.2mg/dl)	0.4	0.4	0.19
LDH (5-248 U/l)	1630	1850	2444
Uric acid (2.6-6 mg/dl)	8	11.2	14.5
Albumin (3.4-5 mg/dl)	2.6	2.41	2.01
INR (0.8-1.3)	1,09	1,4	2.6
CA 19.9 (0-39 U/ml)	578	-	-
CA 125 (0-35 U/ml)	55.73	-	-
Blood culture	No growth	No growth	No growth
Urea culture	No growth	No growth	No growth
Peripheral smear	-	Burkitt's-like cells	-

INR = international normalized rate, AST = aspartate aminotransferase, CRP = C-reactive protein, LDH = lactate dehydrogenase, CA = cancer antigen, HCV = hepatitis C virus, RNA = ribonucleic acid, HbsAg = hepatitis B surface antigen, HIV = human immunodeficiency virus



operative increase in international normalized ratio starting the bleeding diathesis caused by a probable bone marrow infiltration (Table 1).

Chemotherapy and radiation therapy are very effective in Burkitt's lymphoma treatment, while surgery is required only for the treatment of developed complications [24]. The surgical indication in this case is the development of gallbladder perforation. The development of this condition increasing the risk of mortality and morbidity has warranted an emergency laparotomy.

## CONCLUSION

Gallbladder perforation is a rare disease but has a high rate of mortality and morbidity when left untreated. One of the causes of gallbladder perforation is the disorder directly infiltrating the gallbladder wall. Also in this case, Burkitt's lymphoma caused perforation by infiltrating gallbladder wall as the extranodal site of involvement. In conclusion, the clinicians should keep in mind that Burkitt's lymphoma might be a rare cause of gallbladder perforation, and also mortality and morbidity rates in the treatment period might be high depending on the magnitude of the systemic involvement.

### *Informed consent*

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

### *Conflict of interest*

The author declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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