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【 CASE REPORT 】

A Gas-forming Liver Abscess with Massive Bleeding into the Abscess Cavity Due to a Ruptured Inferior Phrenic Artery

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Abstract:
An 88-year-old woman developed a huge abscess, forming an air-fluid level in the right lobe of the liver. A pigtail catheter was placed and drained thick pus with putrid odor from the abscess cavity. Gram-positive rods were detected in the pus, which were subsequently determined to be *Clostridium perfringens* by culture. She developed hemorrhaging in the abscess cavity when the right inferior phrenic artery was damaged by inflammation that had spread from the abscess. Emergency transarterial embolization with gelatin sponges was performed, and the bleeding ceased. We herein report a rare case of liver abscess that caused inferior phrenic artery injury, resulting in bleeding.

Key words: liver abscess, *Clostridium perfringens*, massive arterial bleeding, inferior phrenic artery

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Introduction

Pyogenic liver abscesses are associated with gas formation in 5.6% to 31.8% of cases (1). Approximately 68% of gas-forming liver abscesses are caused by *Klebsiella pneumoniae*, followed by *Escherichia coli*, with a very low incidence of induction by *Clostridium perfringens* (2). *C. perfringens* infection causes hemolysis, leading to a critical condition (3, 4). Thus, its early diagnosis is essential to avoid severe complications.

The diagnosis of *C. perfringens* as the cause of infection is challenging because these bacteria are natural inhabitants of the intestine and vagina in humans. One uncommon complication of liver abscess is bleeding of the hepatic arteries due to pseudoaneurysm (5). Inflammation of the abscess spreads and damages arteries, leading to bleeding. However, there have been no reports of bleeding from arteries other than those in the liver in association with liver abscess.

We herein report a case of gas-forming liver abscess caused by *C. perfringens*, resulting in bleeding into the abscess cavity due to right inferior phrenic arterial injury.

Case Report

An 88-year-old woman was referred to our division with a large cystic lesion in the right lobe of the liver. Abdominal computed tomography (CT) showed a massive abscess 15.5 cm in size that contained an air-fluid level in the right lobe of the liver. She had a medical history of total hip replacement surgery at 76 years old. She was on medication for type 2 diabetes, hypertension, hyperlipidemia, and hypothyroidism. She had slight epigastric discomfort at the referral but did not show any other symptoms, such as abdominal pain, nausea, or diarrhea.

At a physical examination, she showed conjunctival icterus, but her body temperature, blood pressure, pulse rate, and respiratory rate were intact. The laboratory tests suggested intense inflammation with increased white blood cell (WBC) count and C-reactive protein (CRP). She also showed severe liver injury with elevated levels of bilirubin and liver enzymes (Table). She had normocytic anemia with a hemoglobin level of 8.0 g/dL and a mean corpuscular volume of 96 fL. We considered the anemia to be secondary to

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Table. Clinical Characteristics on Admission.

White blood cells (/μL)	50,600
Red blood cells (×10⁴/μL)	281.0
Hemoglobin (g/dL)	8.0
Hematocrit (%)	25.5
MCV (fL)	90.8
MCH (pg)	28.4
MCHC (%)	31.3
Platelet (×10⁴/μL)	25.0
Prothrombin time (%), INR	52.4%, 1.52
APTT (s)	38.6
FDP (μg/mL)	14.2
Antithrombin-III (%)	67.0
Total bilirubin (mg/dL)	4.7
Direct bilirubin (mg/dL)	3.7
AST (IU/L)	1,209
ALT (IU/L)	696
LDH (IU/L)	639
ALP (IU/L)	803
γ-GTP (IU/L)	41
Total protein (g/dL)	4.9
Albumin (g/dL)	1.5
Glucose (mg/dL)	99
Hemoglobin A1c (%)	6.2
Urea nitrogen (mg/dL)	34.0
Creatinine (mg/dL)	1.08
Sodium (mEq/L)	133
Potassium (mEq/L)	5.2
Chloride (mEq/L)	104
C-reactive protein (mg/dL)	23.6
Procalcitonin (ng/mL)	5.71

MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, APTT: activated partial thromboplastin time, FDP: fibrin-fibrinogen degradation products, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, ALP: alkaline phosphatase, γ-GTP: γ-glutamyl transpeptidase

persistent infection and liver injury. Her elevated bilirubin level was predominantly direct bilirubin; however, her aspartate aminotransferase (AST) level was extremely high compared to the levels of alanine aminotransferase (ALT), and her lactate dehydrogenase (LDH) and serum potassium levels were also increased. Although hemolytic anemia could not be ruled out, we presumed that the disease was not severe enough to induce a critical condition.

Abdominal CT showed a large abscess 15.5 cm in diameter that contained gas and fluid forming an air-fluid level in the right lobe of the liver (Fig. 1). We detected no bile duct abnormalities as the possible cause of jaundice. Ultrasound-guided percutaneous drainage of the abscess was performed on admission, wherein a 7.0-French pigtail catheter was inserted into the abscess cavity through a right intercostal space (Fig. 2A). A total of 120 mL of thick, brown, purulent fluid with a putrid odor was drained from the abscess cavity. Intravenous administration of biapenem, a broad-spectrum antibiotic, was started immediately. A microscopic examination of the pus with Gram staining detected large Gram-positive, rod-shaped bacteria (Fig. 2B).

Given the gas formation and Gram-positive rods, we suspected Clostridia infection as the cause of the liver abscess and started the intravenous administration of Clindamycin and Metronidazole in combination. A bacterial culture of the pus subsequently identified *C. perfringens*. We diagnosed the patient with a gas-forming massive liver abscess caused by *C. perfringens*. Her jaundice and ALT elevation suggested severe organ damage caused by *C. perfringens* infection. The pus was highly viscous and drained very slowly through the pigtail catheter. We injected 20 to 40 mL of saline through the catheter twice a day.

Fourteen days after the drainage catheter placement and intravenous administration of antibiotics, the patient's WBC count returned to the normal level, and her CRP level markedly decreased. Her jaundice was resolved, and the ALT level decreased to within the normal limit (Fig. 3); however, the cavity of the abscess remained 13.6 cm in diameter, filled with a fluid-like component and the gas forming the air-fluid level.

Twenty-six days after the drainage catheter placement, she developed a sudden loss of consciousness. Although head CT revealed no abnormalities, abdominal CT detected hemorrhaging in the cavity coming from a branch of the right inferior phrenic artery. Inflammation spreading from the abscess cavity to the diaphragm might have damaged the artery (Fig. 4). The drainage catheter was located at the dorsal side of the abscess cavity some distance from the bleeding site (Fig. 4), so vascular damage due to contact with a long-term-placed drainage tube seemed unlikely.

Emergency angiography detected contrast extravasation from the right inferior phrenic artery (Fig. 5). A branch of the right inferior phrenic artery showed oozing hemorrhaging and a round, enhanced lesion, suggesting a pseudoaneurysm (Fig. 5B, C). A microcatheter was placed in the right inferior phrenic artery, and spherical gelatin sponges 1 mm in diameter were administered until the flow of contrast agent into the abscess cavity disappeared. After successful embolization, the patient's state of consciousness stabilized without rebleeding.

We continued administering antibiotics for another 16 days until the fluid stopped draining from the catheter tube. Follow-up CT showed that the abscess cavity was still present in the liver, with a size of 11.7 cm, but the gas that had been forming the air-fluid level had disappeared (Fig. 6). The abscess cavity was still occupied by a substance similar to pus and containing small, low-density areas of air. We suspected the substance with small air bubbles in the abscess cavity to be solidified purulent fluid. The infection seemed to have been resolved, as the WBC count and CRP level had almost normalized, so we removed the drainage

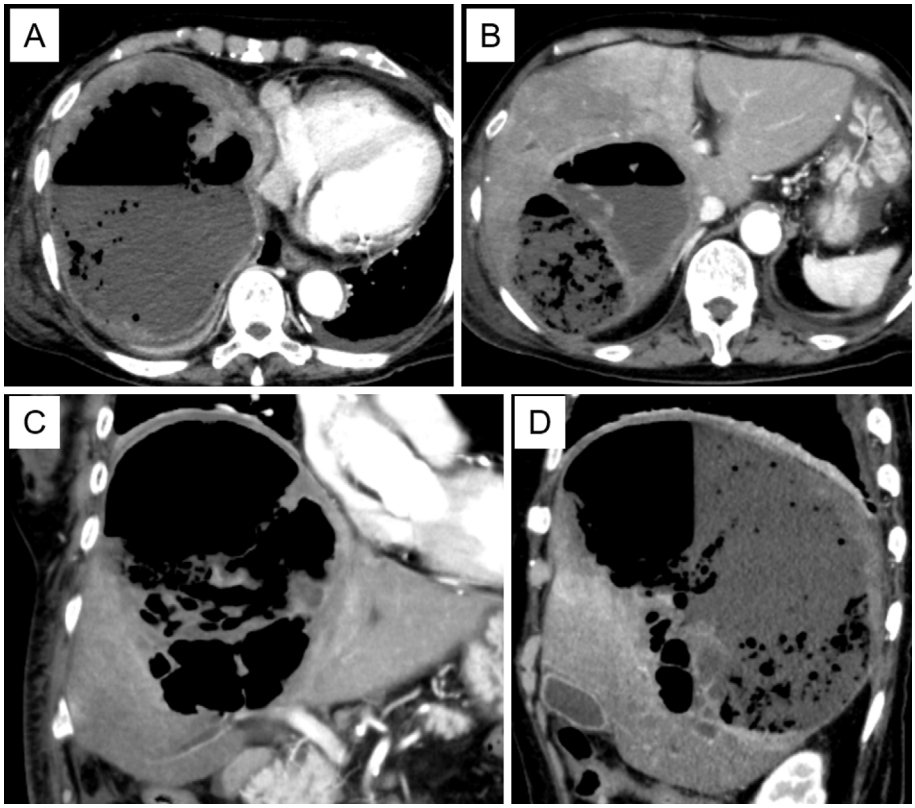

Figure 1. **Abdominal CT images at referral to our division. A large abscess 15.5 cm in size containing gas and fluid, forming an air-fluid level, was located in the right lobe of the liver. (A) Axial image, cephalic level. (B) Axial image, caudal level. (C) Coronal image. (D) Sagittal image.**

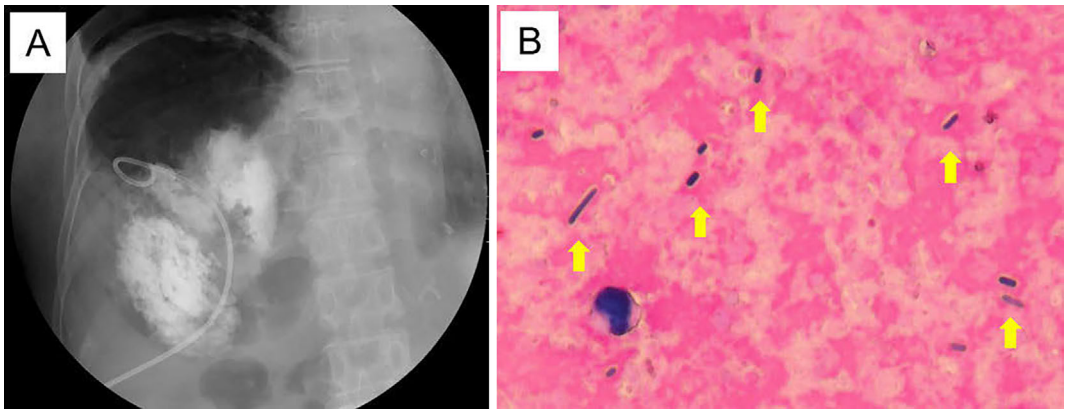

Figure 2. **Fluoroscopic image of the abscess cavity and microscopic images of the pus with Gram staining. (A) Fluoroscopic image of the abscess with pigtail drainage catheter and injected contrast media. (B) Microscopic image of the pus with Gram staining. Large, Gram-positive, rod-shaped bacteria were detected in the pus (arrows).**

catheter tube. The intravenous antibiotic was changed to oral levofloxacin for two weeks.

The patient remained stable after discontinuing oral levofloxacin without a relapse of inflammation (Fig. 3). She was discharged from our hospital 12 days after oral levofloxacin withdrawal and transferred to the referral hospital for rehabilitation. We confirmed that her CRP level had returned to normal 26 days after she moved to the referral hospital.

Discussion

C. perfringens is a normal enteric and vaginal inhabitant in humans and animals and is widely distributed in soil as well as fresh and salt water. *C. perfringens* is a Gram-positive, anaerobic, rod-shaped bacteria that causes gas gangrene. It produces alpha-toxin and perfringolysin O, which are believed to induce the development of gas gangrene in soft tissues (6). In addition to gas gangrene, the most com-

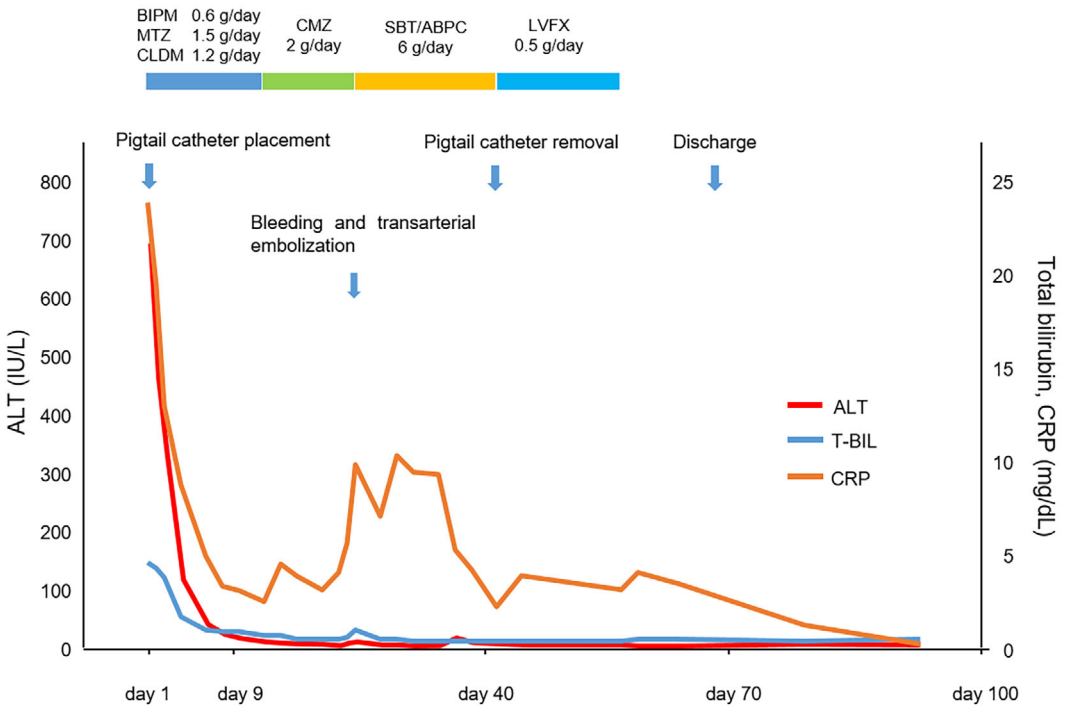

Figure 3. **Clinical course. ALT: alanine aminotransferase, T-BIL: total bilirubin, CRP: C-reactive protein, BIPM: biapenem, MTZ: metronidazole, CLDM: clindamycin, CMZ: cefmetazole, SBT/ABPC: sulbactam/ampicillin, LVFX: levofloxacin**

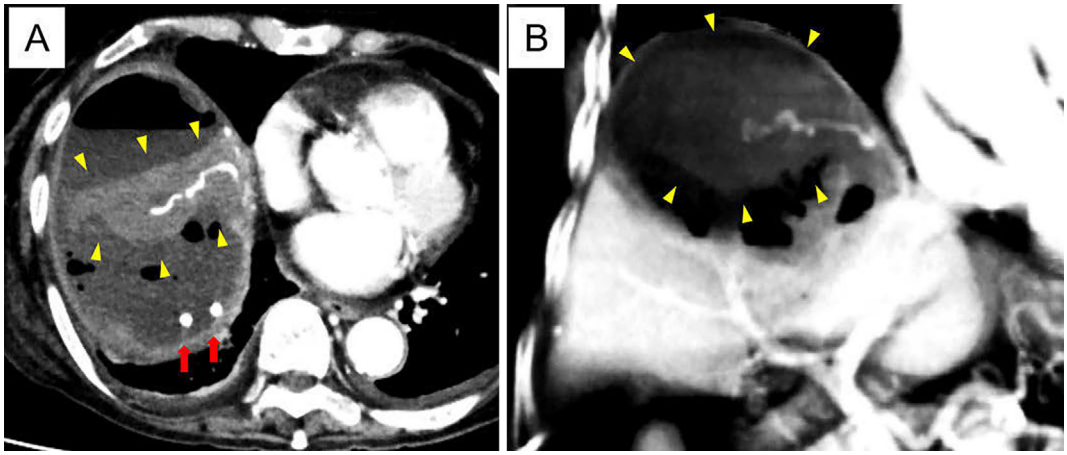

Figure 4. **Abdominal CT images during hemorrhaging. Mild hyperdensity substances indicating bleeding from the right inferior phrenic artery were detected in the abscess cavity (arrowheads). Cross-sections of the pigtailed drainage catheter can be seen (red arrows). (A) Axial image. (B) Coronal image.**

mon disease caused by *C. perfringens* is foodborne disease, and liver abscess is extremely rare (7). *K. pneumoniae* and *E. coli* are the leading causes of gas-forming liver abscess, with *Clostridium* species a rare cause (8). The most common infecting route of liver abscess is through the bile ducts and portal vein. Since *C. perfringens* is a normal inhabitant in the gastrointestinal tract, the infection in the present case appears to have occurred via the biliary tract or portal vein. The present patient did not have any risk factors for bacterial translocation, such as biliary disease, enterocolitis, or colon cancer. She was an older compromised host with pre-existing diseases, such as type 2 diabetes, which may have caused her to develop the liver abscess with *C. perfringens*.

Liver abscesses caused by *C. perfringens* has an extremely poor prognosis (9, 10). It can induce jaundice due to severe hepatocyte injury and is often fatal, causing acute massive intravascular hemolysis (11-13). Kwon et al. reported that hemolysis occurs in 70% of liver abscesses caused by *C. perfringens*, and the mortality rate is 68% (14). Although the prompt initiation of treatment is crucial, an early diagnosis is challenging because bacterial culture identification of *C. perfringens* usually takes several

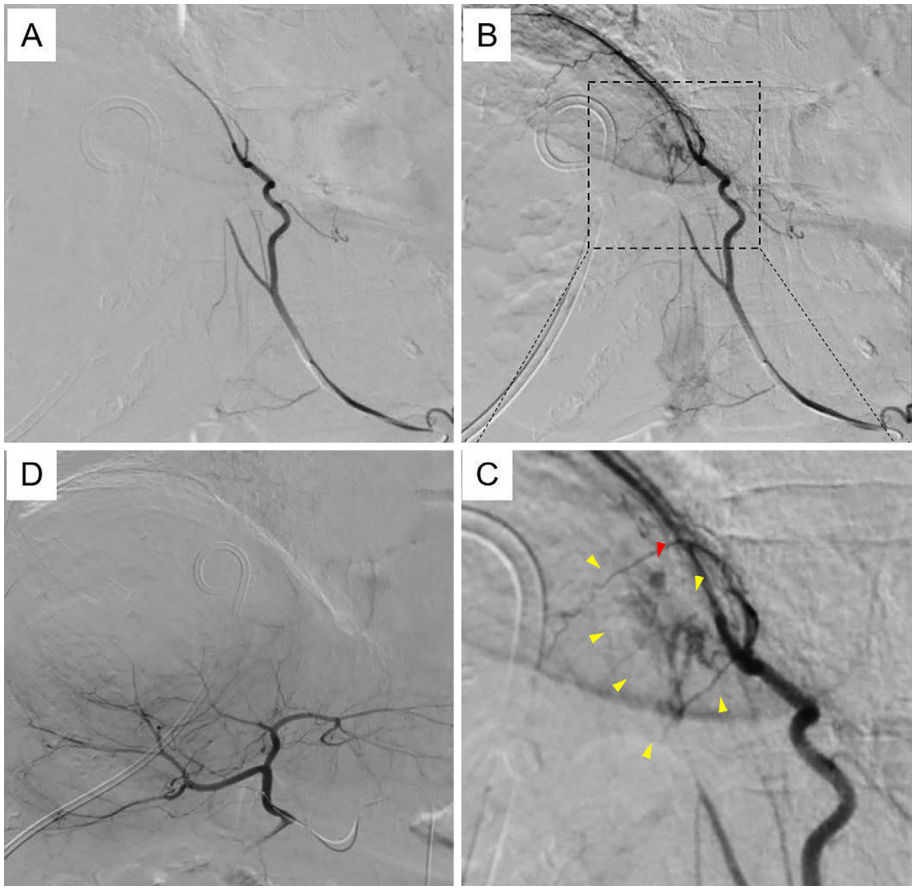

Figure 5. **Digital subtraction angiography. (A) Right inferior phrenic artery (RIPA) angiogram, early phase. (B, C) RIPA angiogram in the late phase showing contrast extravasation. A branch of the right inferior phrenic artery showed oozing hemorrhaging (yellow arrowheads) and a round, enhanced lesion, suggesting a pseudoaneurysm (red arrowhead). (D) Proper hepatic artery angiogram.**

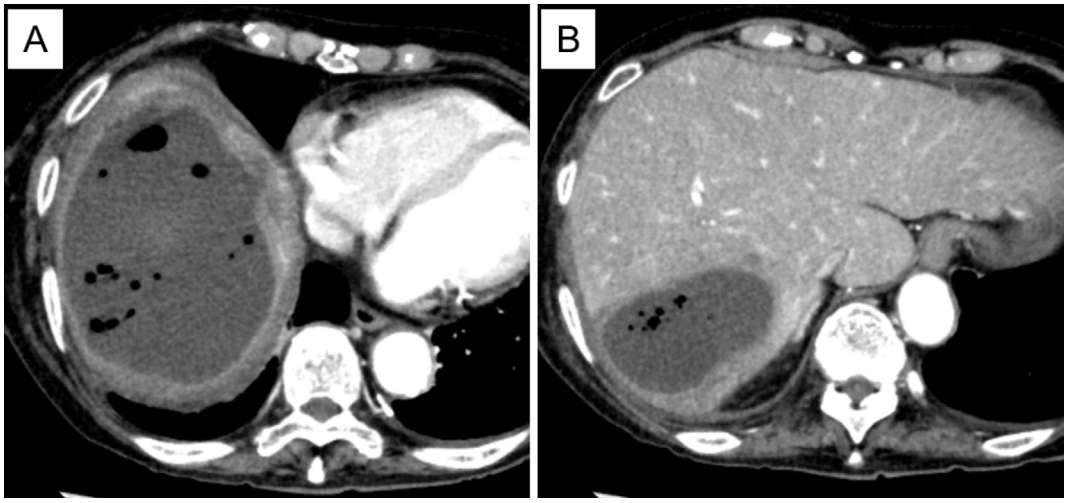

Figure 6. **Abdominal CT images at the removal of the drainage catheter. The abscess cavity is filled with a substance containing small air bubbles. The gas that had formed the air-fluid level is no longer present. (A) Axial image, cephalic level. (B) Axial image, caudal level.**

days. An early diagnostic clue may be Gram staining. *K. pneumoniae* and *E. coli*, the main causative bacteria of gas-forming liver abscesses, are Gram-negative rods, whereas *C. perfringens* is a Gram-positive rod. In the present case, Gram staining identified large, Gram-positive rods before the identification with pus culture, and given the gas-formation, we suspected *C. perfringens* infection and were able to initiate the administration of appropriate antibiotics.

The prediction of *C. perfringens* by Gram staining may be essential for the prompt treatment of *C. perfringens* infection.

The prognosis of patients with septicemia caused by *C. perfringens* is extremely poor, with a 70-100% mortality due to massive hemolysis caused by the alpha-toxin (3). The hemolysis is mainly caused by the disruption of erythrocyte membranes due to the phospholipase C activity of alpha-toxin (6). A peripheral blood smear of the hemolysis shows spherocytes, ghost cells, and cyst cells (12, 13). Elevated levels of indirect bilirubin, LDH, and potassium in the serum support the detection of hemolysis. In the present case, the bilirubin level was elevated, but it was predominantly direct bilirubin. Her peripheral blood smear did not show spherocytes or ghost cells, indicating no evidence of massive hemolysis.

Treatment of liver abscesses caused by *C. perfringens* is based on drainage and antibiotic administration. Percutaneous drainage should be promptly performed for the gas-forming liver abscess. Liver abscesses caused by *C. perfringens* tend to rupture because of the vulnerable abscess cavity wall weakened by hepatocyte injury and increased internal pressure due to gas formation (15). Drainage or surgical removal of the abscess improves the prognosis (10). In general, percutaneous drainage is the first step in treating pyogenic liver abscesses, followed by more invasive surgical drainage or resection if this approach is not successful. *C. perfringens* pus can be a highly viscous fluid, so drainage may not be effective. In such cases, surgical treatment should be considered without delay. In the present case, the pus was too viscous to drain spontaneously through the placed drainage catheter. Since the patient was too old with too many complications to undergo hepatectomy, we continued flushing the catheter tube with saline. Although the abscess cavity did not disappear, the abscess fluid did solidify with long-term antibiotics administration.

C. perfringens is susceptible to penicillins, cephems, and carbapenems, but clindamycin and metronidazole have been reported to be superior at inhibiting the activity of toxins produced by *C. perfringens* at an early stage (16). Combining these drugs with penicillins, cephems, or carbapenems may be useful for preventing hemolysis from causing a critical condition (10, 16). In the present case, a carbapenem was started immediately after admission, and when Gram-positive rods were detected in the pus, we suspected *Clostridium* infection and started administrating clindamycin/metronidazole. Although the *C. perfringens* in this case may have been a strain with an alpha-toxin activity too low to cause hemolysis, the early initiation of appropriate antibiotics administration might have been the reason for the lack of massive hemolytic anemia.

In this case, bleeding into the abscess occurred due to the disruption of the right inferior phrenic artery during the clinical course. A markedly increased internal pressure due to gas formation and the spread of inflammation to the diaphragm may have caused the collapse of a branch of the right inferior phrenic artery. Bleeding in visceral arteries mainly occurs in splenic arteries, followed by hepatic arteries, and is rare in the inferior phrenic arteries (17, 18). The causes of bleeding in the inferior phrenic artery consist of pseudoaneurysms induced by mechanical injury including surgical procedures and vulnerable arteries induced by spreading inflammation due to pancreatitis or other entities (19). However, visceral arterial bleeding reports related to liver abscesses are limited to those involving hepatic arteries that often induce biliary bleeding. The spread of inflammation from the abscess generates pseudoaneurysm formation in hepatic arteries, resulting in bleeding (5). There have been no reports of inferior phrenic artery bleeding due to liver abscesses, suggesting that the spread of inflammation may be generally limited to the liver. In the present case, the abscess was located in the posterior segment close to the diaphragm, resulting in the spread of the inflammation to the diaphragm.

In conclusion, we encountered a rare case of gas-forming liver abscess caused by *C. perfringens* near the diaphragm, resulting in bleeding into the abscess cavity due to rupture of the inferior phrenic artery. Physicians should keep in mind that a liver abscess in the adjacent diaphragm can cause arterial bleeding.

Informed consent was obtained from the patient for publishing.

The authors state that they have no Conflict of Interest (COI).

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