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Case report

Non-traumatic gas gangrene in the abdomen: report of six autopsy cases

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Abstract: Six autopsy cases of non-traumatic gas gangrene in the abdomen are reported. Five of the six were caused by *clostridia*, as identified by culture or histology. There were associated underlying diseases, such as alcoholism, liver cirrhosis, diabetes mellitus, and malignant disease. Three of the six patients had gas gangrene in the liver. Bacterial proliferation and gas accumulation were found in the sinusoids of the liver, and congestion and edema with extensive gas embolism were found in the lungs. Pulmonary gas embolism was considered to be the direct cause of death in these three patients. The other three patients had intestinal clostridial gas gangrene, with alcoholism as an underlying condition. None of the six patients was clinically diagnosed as having gas gangrene. We suggest that gas gangrene should be considered in any patient with abdominal infection. A review of 19 autopsy cases of gas gangrene in the abdomen reported in the Japanese literature is also presented.

Key words: non-traumatic gas gangrene, *clostridium*, autopsy case, electron microscopy

Introduction

Classically, gas gangrene was known to be associated mostly with trauma and caused by clostridial infection.[1,2] It has also been reported to occur in the absence of trauma or surgical procedures, and gas gangrene without external injury is, therefore, called non-traumatic gas gangrene.[3,4] Most non-traumatic gas gangrene is associated with underlying diseases which cause immunodeficiency, such as malignancy,[3–12] hematological disease,[12–16] and diabetes mellitus.[3–10,17–20] Non-traumatic gas gangrene is rare, but often rapidly progressive, and requires emergent care. Early diagnosis of non-traumatic gas gangrene in the abdomen is often difficult.

We report six autopsy cases of non-traumatic gas gangrene in the abdomen. We also present a review of the Japanese literature of 19 reported autopsy cases of gas gangrene in the abdomen. The features of intrahepatic and intestinal gas gangrene in Japan are summarized. To our knowledge, this is the first article to have summarized autopsy cases of gas gangrene in the abdomen in the Japanese literature. We hope this article will be helpful in improving the knowledge and management of non-traumatic gas gangrene in abdominal organs.

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Case reports

Clinical findings

The clinical findings of the six patients reported are summarized in Table 1.

Cases 1–3 had intrahepatic gas gangrene. Case 1 was a 72-year-old woman who had had a fever and epigastralgia for 2 days before admission. She was diagnosed with acute hepatitis. She received conservative therapy and died 2 days after admission. Case 2, a 71-year-old woman, had had a fever for 2 days and died 4 h after admission. Case 3 was a 70-year-old diabetic woman who had had a fever for 1 day prior to admission. She was clinically diagnosed with infection in the biliary tract. Treatment with antibiotics failed and she died 3 days after admission. Clinically, the sudden death of all these three paitients was attributed to acute respiratory failure.

Cases 4–6 had intestinal clostridial gas gangrene (CGG). Case 4 was a 44-year-old man with the chief complaint of abdominal pain for 2 days; he died 8 h after admission. Case 5 was a 47-year-old man who had had disturbance of consciousness for several hours. He died

Table 1. Clinical summary of the six autopsy cases reported in this study

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age (years)/Sex	72/F	71/F	70/F	44/M	47/M	54/F
Clinical presentation	Fever, vomiting, epigastralgia, respiratory difficulty	Fever, icterus, DOC, general fatigue, respiratory difficulty	Fever, thirst, abdominal pain, respiratory difficulty	Abdominal pain, vomiting, DOC	DOC	Unknown
Underlying diseases	Hypertension, hyperlipemia	Hypertension	DM	Alcoholism	Alcoholism	Alcoholism, LC
Clinical diagnoses	Acute hepatitis	Biliary infection, sepsis, hemolytic anemia	Biliary infection, DKA, DIC	DIC, ARF	Hepatorenal syndrome	DOA
Treatment	Nothing remarkable	Nothing remarkable	Antibiotics	Nothing remarkable	Nothing remarkable	Nothing remarkable
Survival after onset	4 Days	2 Days	4 Days	3 Days	2 Days	1 Day
Laboratory data	WBC 7200/mm^3 RBC 4.14 × 10^6/mm^3 Hb 12.8 g/dl Ht 38.5% Plt 179000/mm^3 ESR 46 mm/h CRP 7.2 mg/dl GOT 742 IU/I GPT 401 IU/l ALP 1128 IU/l LDH 1844 IU/l G-GTP 973 IU/l T.Bil. 2.3 mg/dl D.Bil. N/A BUN 23 mg/dl Cre 0.9 mg/dl Sodium 144 mEq/l Potassium 3.6 mEq/l Chloride 103 mEq/l BS 152 mg/dl S-amylase 68 IU/l BGA (room air) pO_2 15.0 mmHg pCO_2 35.5 mmHg pH 7.220, BE-14.5 HCVAb (+)	WBC 25000/mm^3 RBC 1.48 × 10^6/mm^3 Hb 5.8 g/dl Ht 12.7% Plt 201000/mm^3 ESR N/A CRP 13.1 mg/dl GOT N/A GPT 159 IU/l ALP 875 IU/l LDH N/A G-GTP N/A T.Bil. 20.6 mg/dl D.Bil. 11.9 mg/dl BUN 33.2 mg/dl Cre 1.5 mg/dl Sodium 122 mEq/l Potassium 7.0 mEq/l Chloride 102.1 mEq/l BS 235 mg/dl S-amylase 272 IU/l BGA (room air) pO_2 55.0 mmHg pCO_2 17.7 mmHg pH 7.149, BE-19.9	WBC 11630/mm^3 RBC 4.42 × 10^6/mm^3 Hb 13.7 g/dl Ht 38.7% Plt 109000/mm^3 ESR N/A CRP N/A GOT 196 IU/l GPT 200 IU/l ALP 355 IU/l LDH 559 IU/l G-GTP N/A T.Bil. 1.4 mg/dl D.Bil. 0.7 mg/dl BUN 27.6 mg/dl Cre 0.5 mg/dl Sodium 130 mEq/l Potassium 3.6 mEq/l Chloride 90 mEq/l BS 371 mg/dl S-amylase 29 IU/l BGA (room air) pO_2 62.1 mmHg pCO_2 19.2 mmHg pH 7.293, BE-14.6	WBC 12000/mm^3 RBC 3.98 × 10^6/mm^3 Hb 14.3 g/dl Ht 40.4% Plt 31000/mm^3 ESR N/A CRP 1+ GOT 443 IU/l GPT 117 IU/l ALP N/A LDH 912 IU/l G-GTP N/A T.Bil. N/A D.Bil. N/A BUN 32.8 mg/dl Cre 4.8 mg/dl Sodium 128 mEq/l Potassium 4.6 mEq/l Chloride 82 mEq/l BS N/A S-amylase 766 IU/l BGA (FiO_2 = 0.4) pO_2 173.5 mmHg pCO_2 59.1 mmHg pH 6.877, BE-27.0	WBC 6700/mm^3 RBC 4.55 × 10^6/mm^3 Hb 14.8 g/dl Ht 41.3% Plt N/A ESR N/A CRP 1.08 mg/dl GOT 6310 IU/l GPT 708 IU/l ALP 508 IU/l LDH 7310 IU/l G-GTP 1066 IU/l T.Bil. 3.4 mg/dl D.Bil. 2.2 mg/dl BUN 45.1 mg/dl Cre 1.5 mg/dl Sodium 129 mEq/l Potassium 4.6 mEq/l Chloride 79 mEq/l BS N/A S-amylase 578 IU/l BGA (FiO_2 = 0.4) pO_2 149.8 mmHg pCO_2 18.1 mmHg pH 6.852, BE N/A	WBC 17100/mm^3 RBC 3.48 × 10^6/mm^3 Hb 12.2 g/dl Ht 34.8% Plt 16000/mm^3 ESR N/A CRP N/A GOT 336 IU/l GPT 210 IU/l ALP N/A LDH 3556 IU/l G-GPT N/A T.Bil. N/A D.Bil. N/A BUN 77.4 mg/dl Cre 6.8 mg/dl Sodium 128 mEq/l Potassium 3.9 mEq/l Chloride 84 mEq/l BS N/A S-amylase N/A BGA N/A

DOC, disturbance of consciousness; DM, diabetes mellitus; LC, liver cirrhosis; DKA, diabetic ketoacidosis; DIC, disseminated intravascular coagulation; ARF, acute renal failure; DOA, dead on arrival; WBC, white blood cell count; RBC, red blood cell count; Hb, hemoglobin; Ht, hematocrit; Plt, platelet count; ERS, erythrocyte sedimentation rate; CRP, C-reactive protein; ALP, alkaline phosphatase; LDH, lactate dehydrogenase; G-GTP, gamma-glutamyle transpeptidase; T.Bil., total bilirubin; D.Bil., direct bilirubin; BUN, blood urea nitrogen; Cre, creatinine; BS, blood sugar; s-amylase, serum amylase; BGA, arterial blood gas analysis; FiO_2, oxygen concentration of inspiratory gas; BE, base excess; HCVAb, hepatitis C viral antibody; N/A, not available

2 days after admission. Case 6 was a 54-year-old woman with a history of alcoholic liver cirrhosis. She was pronounced dead on arrival at the hospital. Her chief complaint was unknown. Alcoholism and alcoholic liver injury were underlying conditions in all three of these patients.

Abdominal ultrasound (US) was performed in case 1 and case 3. High echoic liver was detected in case 1; this was considered to indicate fatty liver. There was no such finding in case 3. Abdominal computed tomography (CT) was not performed in any of the six patients. None of the six patients was clinically diagnosed with gas gangrene, and all six patients died within 4 days after the onset.

Pathological findings

Table 2 is a summary of the pathological findings in the six patients. In case 1, the liver appeared swollen, with spongy softening lesions at autopsy (Fig. 1). Histological observation revealed proliferation of gram-positive bacilli in the focally dilated sinusoids (Fig. 2a,b) and lymphocyte infiltration around the intrahepatic bile ducts (Fig. 3). Scanning electron microscopic examination showed that the bacilli in the liver sinusoid were about 3- to 9-μm-long and 0.9- to 1.3-μm-wide, and they had a large "box-car" shape with blunt ends and were without flagella (Fig. 4). The bacilli were histologically consistent with *Clostridium (Cl.) perfringens*.[21] Case 2 and case 3 had liver lesions similar to those in case 1 at autopsy. Figure 5 shows the gross features of the liver in case 3. Proliferation of gram-positive bacilli, considered histologically to be *clostridia*, was found in case 2. However, in case 3, the proliferation of gram-negative bacilli was observed in histological sections. A papillary tumor, 1.8 × 1.4 × 1.0 cm in size, was detected at Vater's papilla at autopsy. It was histologically well differentiated adenocarcinoma without necrosis or submucosal invasion. In all three of these patients, the lungs showed congestion and edema, with diffuse gas emboli (Fig. 6).

In cases 4 and 5, the small intestines showed necrosis and dilation at autopsy. *Cl. perfringens* was successfully cultured from both cadaveric blood and the small-intestinal mucosa obtained at autopsy in both patients. Histological observation of the small intestines revealed mucosal necrosis with proliferation of gram-positive bacilli, many bubbles in the submucosa, and dilation of the veins (Fig. 7a,b). In addition, necrotizing pancreatitis was also noted in both patients. In case 6, a gas gangrene lesion was found in the ileocecal region at autopsy. *Cl. perfringens* was cultured from cecal mucosa obtained at autopsy. Histological findings were similar to those of intestinal CGG in cases 4 and 5. The kidneys showed gangrene in the parenchyma, with many bubbles, inflammatory cells, hemorrhage, and proliferation of gram-positive bacilli. Features of alcoholic cirrhosis were found in the liver.

Fig. 1. Gross appearance of the liver in case 1. The liver shows spongy softening lesions

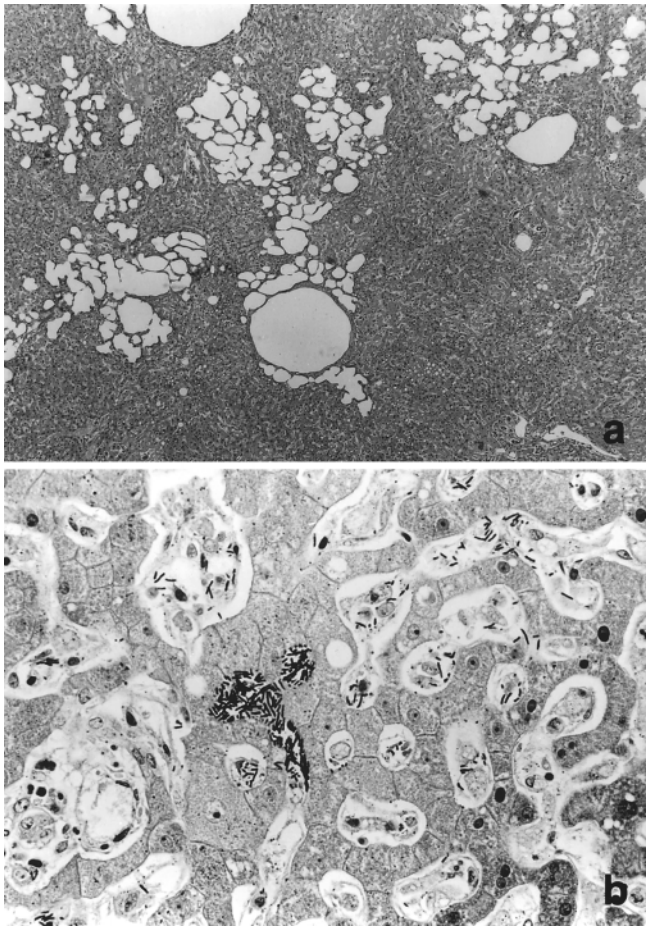

Fig. 2a,b. Microscopic features of the liver in case 1. **a** Focally dilated sinusoids. **b** Gram-positive bacilli in the sinusoids **a** H&E, ×10. **b** Gram stain, ×100

Table 2. Summary of pathological findings in the six autopsy cases reported in this study

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Location of gas gangrene	Liver	Liver	Liver	Small intestine	Small intestine	Intestine, kidney
Pathogen	*Cl. perfringens*	*Clostridium*	Gram-negative rod	*Cl. perfringens*	*Clostridium*	*Cl. perfringens*
Culture of autopsy materials	Not performed	Not performed	Not performed	Small intestine, blood	Small intestine, blood	Cecum
Pathological findings						
Liver	Gas gangrene, fatty liver, viral hepatitis, cholangitis	Gas gangrene	Gas gangrene	Fatty liver with fibrosis	Fatty liver	Alcoholic liver cirrhosis
Intestine	Preserved	Preserved	Adenocarcinoma at Vater's papilla	Gas gangrene	Gas gangrene	Gas gangrene
Kidneys	Swelling	Swelling	Fibrin thrombi in glomeruli	Swelling, congestion	Swelling, congestion	Gas gangrene
Lungs	Gas embolism, congestion and edema	Gas embolism, congestion and edema	Gas embolism, congestion and edema	Hemorrhage in the left lung	Congestion	Congestion
Pancreas	Preserved	Preserved	Chronic pancreatitis, moderate	Necrotizing pancreatitis	Necrotizing pancreatitis	Acute pancreatitis, mild
Histological bacteremia	Present	Present	Absent	Present	Present	Present
Other	Choledochal stones, atherosclerosis of aorta, mild	Atherosclerosis of aorta, severe	Chronic cholecystitis with stones, mild, hemorrhagic gastric ulcers	NP	NP	Hemorrhagic gastric erosions
Main cause of death	Pulmonary gas embolism, sepsis	Pulmonary gas embolism, sepsis	Pulmonary gas embolism, DIC	Necrotizing pancreatitis, sepsis	Necrotizing pancreatitis, sepsis	ARF

NP, nothing particular; DIC, disseminated intravascular coagulation; ARF, acute renal failure

Discussion

All six patients in this report had non-traumatic gas gangrene, and five of them had CGG. The anaerobic bacteria group that consists of 90 species known as the genus *Clostridium* was first described in 1861 by Louis Pasteur.[22] *Clostridia* are widely distributed in nature. They can be found in soil, dust, and water, and in the intestines of humans and animals. So far six species of *clostridia* have been reported to cause gas gangrene in humans.[23–25]

We reviewed the Japanese literature and found that 19 autopsy cases of gas gangrene in the abdomen had been reported, as summarized in Table 3. There were 15 cases of intrahepatic gas gangrene and 5 cases of intestinal CGG. There were 2 cases which had both intrahepatic and intestinal CGG. Ten cases (52.6%) were considered to be non-traumatic CGG, and nine of the ten patients died within 4 days after the onset. The most frequent pathogen in traumatic CGG has been thought to be *Cl. perfringens* and that in non-traumatic CGG, *Cl. septicum*.[26] However, nine of the ten cases of

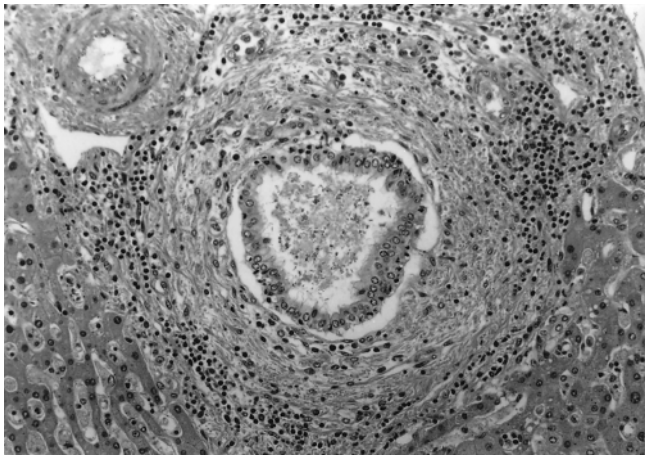

Fig. 3. Microscopic appearance of the intrahepatic bile duct in case 1. Note lymphocyte infiltration around the bile duct. H&E, ×50

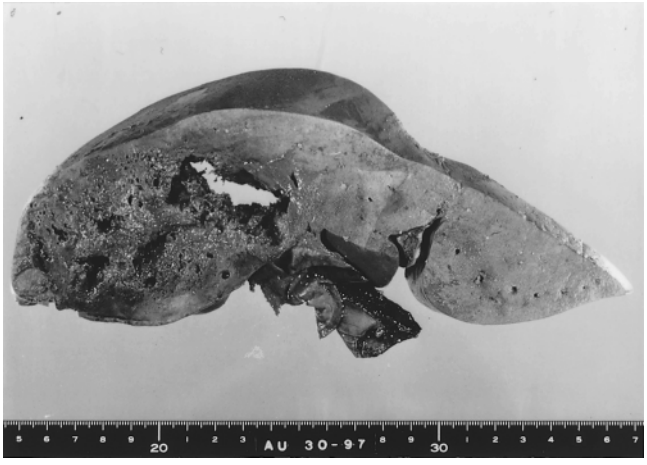

Fig. 5. Gross appearance of the liver in case 3. Note necrotic lesion with spongy softening in the right lobe

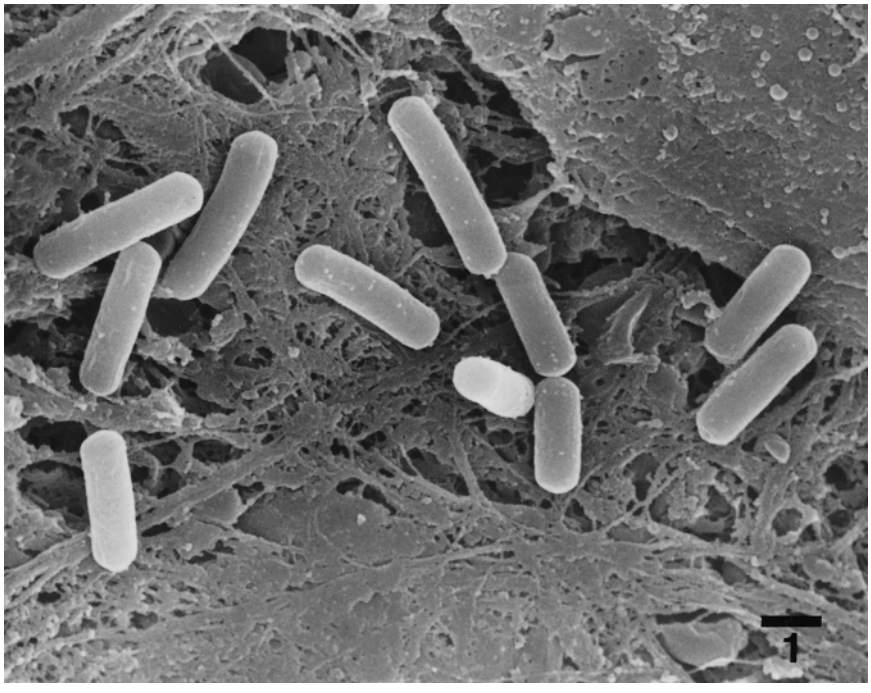

Fig. 4. Scanning electron microscopic demonstration of liver sinusoid in case 1. Note several large "box-car"-shaped bacilli with blunt ends and without flagella. *Bar* is 1 μm

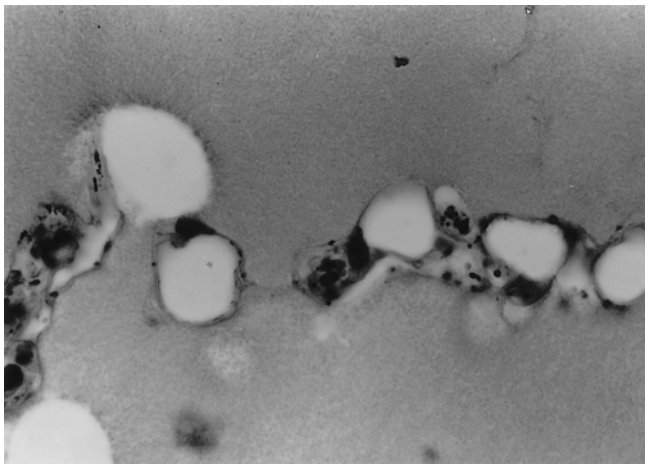

Fig. 6. Microscopic appearance of the alveolar wall in case 1. Note several dilated capillaries. H&E, ×100

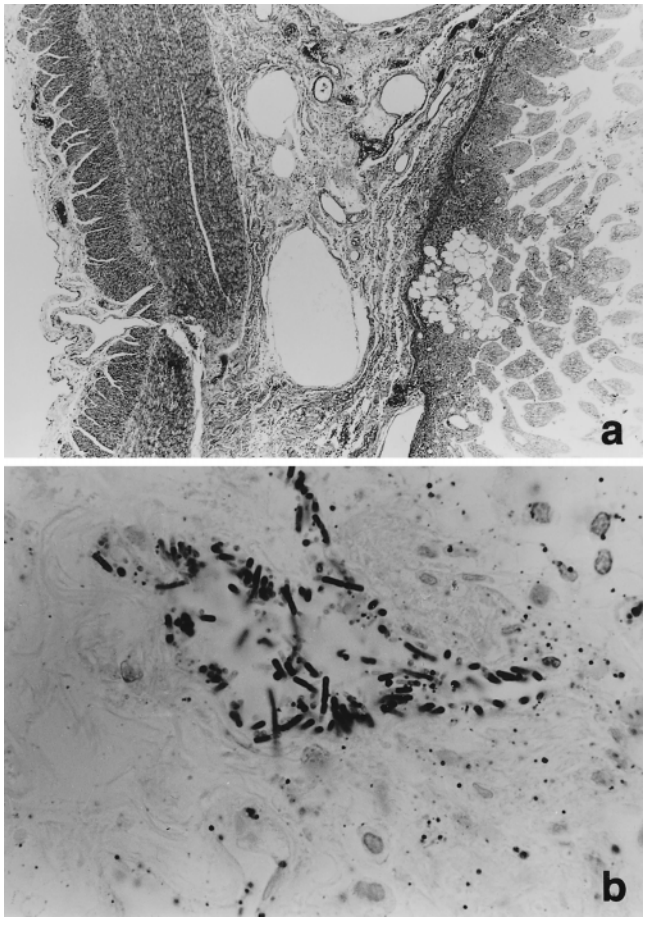

Fig. 7a,b. Microscopic appearance of the small intestine in case 4. **a** Note mucosal necrosis and many bubbles. **b** Note gram-positive bacilli in the wall. **a** H&E, ×10. **b** Gram stain, ×250

non-traumatic CGG reported in the Japanese literature, were caused by *Cl. perfringens*. In our series, three of the five CGG cases were also caused by *Cl. perfringens*. These findings suggest that *Cl. perfringens* is the most common pathogen in autopsy cases of non-traumatic CGG in the abdomen in Japan. Most autopsy cases of non-traumatic CGG in the Japanese literature were reported to be associated with underlying diseases.

Cases 1–3 in our report had intrahepatic gas gangrene. Clinically, all three patients died suddenly of acute respiratory failure. Pathological examination of the lungs revealed congestion, edema, and extensive gas embolism in all three. It is, therefore, suggested that pulmonary gas embolism was the direct cause of death in these patients. It is conceivable that the bacteria first arrived in the liver sinusoids via either the bile duct or portal vein, and then proliferated and produced much gas there, which finally caused the pulmonary gas embolism. In the cases reported in the Japanese literature, lung congestion and/or edema was described in 5 of the 15 patients with intrahepatic gas gangrene. We believe that pulmonary gas embolism is an important complication in intrahepatic gas gangrene.

Our cases 4–6 had intestinal CGG, with alcoholism as an underlying condition. In the cases reported in the Japanese literature, alcohol abuse was noted in four of the five patients with intestinal CGG. The relationship between alcoholism and intestinal CGG is not very clear. It is known that the diminished degradation of beta toxin by proteases can induce necrotizing enteritis.[27–29] It seems possible that chronic alcohol abuse may have diminished the pancreatic exocrine secretion in these patients. The effects of ethanol on pancreatic exocrine secretion seem to vary under different conditions, such as the duration of ethanol consumption.[30] In an analysis of pure pancreatic juice in alcoholic patients, Harada et al.[31] reported that there was diminished secretion of proteins, including chymotripsinogen, at an advanced stage of chronic alcoholism. Although toxin analyses were not performed in the three patients in our series who had a history of alcohol abuse, the role of beta toxin in intestinal CGG cannot be ruled out. It is apparent that alcohol abuse is an important underlying factor in the induction of intestinal CGG.

US and CT are very useful for making a diagnosis of gas gangrene in the abdomen. In particular, CT often detects even small amounts of gas that cannot be visualized by conventional plain X-ray examination.[32] Unfortunately, none of the present six patients was clinically diagnosed with gas gangrene. Although abdominal US was performed in case 1 and case 3, a diagnosis of gas gangrene was not made in either patient. Abdominal CT was not performed in any of the six patients, and it should have been done. Why were the appropriate

Table 3. Summary of 19 autopsy cases of gas gangrene in the abdomen reported in the Japanese literature

Author	Year	Age (years)/Sex	Class.	Pathogen	Location of GG	Underlying conditions	Clin.Dx.	Treatment	Survival after onset	Remarkable pathological findings
Konishi	1979	52/M	NCGG	*Escherichia coli*	Liver	Gastric ca., operated	Yes	st	12 Days	Bacterial emboli in vessels
Oguma[33]	1987	59/M	?	Rod	Liver	Pancreas ca., operated, liver metastasis, TAE	Yes	n.r.d.	3 Days	Metastatic liver ca., lung edema, gas embolism in cerebrum and cerebellum
Nakano[19]	1988	68/M	CGG, NT	*Cl. perfringens*	Liver	DM	Yes	n.r.d.	1 Day	Lung edema, small foci of GG in pancreas, kidney, bone marrow, and myocardium
Tokita[11]	1988	74/M	CGG, NT	*Cl. septicum*	Liver	Colon ca., liver metastasis	Yes	ab	12 h	Perforation of transverse colon ca., metastatic liver ca.
Mandai[10]	1989	75/M	CGG	*Cl. perfringens*	Liver	DM, HCC, TAE, gastric ca., operated, lung ca., operated	Yes	dr	10 h	Hepatoma, liver metastasis of gastric ca., lung congestion and edema
Mandai[10]	1989	49/M	CGG, NT	*Cl. perfringens*	Abdominal wall-retroperitoneum	Colon ca.	Yes	ab	22 Days	Cecal ca.
Mori[34]	1991	74/F	CGG	*Cl. septicum*	Liver, intestine	Esoph. ca., irradiated, operation	Yes	ab	3 Days	No description of remnant carcinoma
Shiroma	1991	82/F	CGG, NT	*Cl. perfrigens*	Liver	Lung carcinoid	Yes	n.r.d.	2 Days	Lung carcinoid
Morioka[35]	1992	67/M	NCGG	*E. aerogenes*	Liver	DM, PTCD, recurrent gastric ca.	Yes	ab, dr	19 Days	Recurrent gastric ca.
Yoshida[36]	1992	67/F	CGG	*Cl. perfringens*	Liver	Duodenal ca., GB ca., operation	Yes	ab, dr	40 Days	Remnant duodenal ca.
Ihara[37]	1992	55/M	CGG, NT	*Cl. perfringens*	Liver, intestine	DM suspected, alcohol abuse	?	n.r.d.	4 Days	Lung congestion and edema, alcoholic liver injury, necrosis of pancreas
Saito[38]	1993	58/M	NCGG, NT	*K. pneumoniae*	Liver	DM suspected	Yes	ab, st	8 Days	Gas production in many organs, gas embolism in vessels
Ihara[20]	1995	57/M	CGG, NT	*Cl. perfringens*	Intestine	Alcohol abuse	?	n.r.d.	2 Days	Alcoholic liver fibrosis
Ihara[20]	1995	75/M	CGG, NT	*Cl. perfringens*	Intestine	Alcohol abuse	?	n.r.d.	2 Days	Alcoholic liver fibrosis
Ihara[20]	1995	53/M	CGG, NT	*Cl. perfringens*	Intestine	DM, alcohol abuse	?	n.r.d.	2 Days	Alcoholic liver fibrosis
Tohma[39]	1996	77/M	CGG, NT	*Cl. perfringens*	Liver	n.r.d.	Yes	n.r.d.	12 h	Lung congestion and edema
Watanabe	1997	58/M	NCGG	*A. hydrophila*	Liver	LC, HCC, PEIT	Yes	ab	21 Days	n.r.d
Ogawa[40]	1997	45/M	CGG, NT	*Cl. perfringens*	Liver	n.r.d.	Yes	ab	12 h	Bacteria in many organs
Sato	1998	55/F	CGG	*Cl. subterminale*	Liver, spleen, GI tract	Bile duct ca., operated	?	n.r.d.	?	Gas embolism in IVC, peritonitis carcinomatosa

GG, Gas gangrene; Class., classfication of GG; Clin.Dx., clinical diagnosis of GG; CGG, clostridial gas gangrene; NCGG, non-clostridal gas gangrene; NT, non-traumatic gas gangrene; *E., Enterobacter*; *K., Klebsiella*; *A., Aermonomas*; GI, gastrointestinal; esoph., esophagus; GB, gallbladder; ca., carcinoma; DM, diabetes mellitus; HCC, hepatocellular carcinoma; TAE, transcatheter arterial embolization; PTCD, percutaneous transhepatic cholangio-drainage; LC, liver cirrhosis; PEIT, percutaneous ethanol infusion therapy; n.r.d., no remarkable description; st, surgical treatment; ab, antibiotics; dr, drainage; IVC, inferior vena cava

imaging modalities not performed in these patients? Partly because there was not enough time to do so in some patients, but the main reason may be that a possible diagnosis of gas gangrene was not kept in mind at all. There is, therefore, a lesson for us to learn; when we face a patient with likely abdominal infection, it is very important to take the diagnosis of gas gangrene into consideration and to use appropriate imaging modalities.

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