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Case Report

Bacterial peritonitis in a patient with malignant ascites caused by pancreatic carcinoma: Case report and review of literature☆

Hirotaka Miyashita [a], Koh Okamoto [a, *], Tatsuya Kobayashi [a], Yoshitaka Wakabayashi [a], Satoshi Kitaura [a], Kazuhiko Ikeuchi [a], Kazunaga Ishigaki [b], Yosuke Nakai [b], Shu Okugawa [a], Kazuhiko Koike [b], Kyoji Moriya [a]

[a] Department of Infectious Diseases, The University of Tokyo Hospital, Tokyo, Japan
[b] Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

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ABSTRACT

Bacterial peritonitis, an infection of the ascitic fluid, can be classified etiologically as spontaneous or secondary bacterial peritonitis. The former is mainly caused by portal hypertension and its subsequent effects, whereas the latter is caused by the direct dissemination of bacteria into the peritoneal cavity. Previous reports have described some distinguishing features of these two entities. Here, we report the first known case of bacterial peritonitis with *Aeromonas hydrophilia* and *Escherichia coli* in a patient with malignant ascites associated with pancreatic carcinoma who exhibited features of both spontaneous and secondary peritonitis. Our report suggests that clinicians should also consider bacterial peritonitis in patients with malignant ascites who present with ostensibly cancer-related symptoms.

1. Introduction

Spontaneous bacterial peritonitis (SBP) is a bacterial infection of ascitic fluid that occurs almost exclusively in patients with cirrhotic ascites [1]. This condition differs from secondary bacterial peritonitis, which is characterized by the presence of a surgically correctable lesion, such as an intestinal perforation or intra-abdominal abscess. Despite the etiological differences, however, it may be difficult to distinguish these types of peritonitis. Here, we report a case of bacterial peritonitis with features of both spontaneous and secondary bacterial peritonitis.

2. Case report

A 64-year-old Japanese man with metastatic pancreatic carcinoma, malignant ascites, and poorly controlled type 2 diabetes presented with a 2-day history of fever and abdominal distention. Two months earlier, he had been diagnosed with pancreatic carcinoma based on a pathologic analysis of a specimen obtained via endoscopic ultrasound fine needle aspiration of the lesion in the pancreatic head. Prior to this diagnosis, he had smoked 40 cigarettes and consumed 1 L of beer per day since the age of 20 years. Intravenous contrast-enhanced computed tomography (CT) of the abdomen revealed a pancreatic mass without portal vein invasion, multiple metastases in the liver and intraabdominal lymph nodes, and peritoneal carcinomatosis without cirrhosis or splenomegaly. Chemotherapy with gemcitabine and nab-paclitaxel was initiated.

Four weeks into the first course of chemotherapy, the patient developed a fever and abdominal tenderness. A complete blood count indicated no myelosuppression. An ascitic fluid analysis revealed a white blood cell count of 700/μL and polymorphonuclear cell count of 119/μL (Table 1). Cytology revealed malignant cells consistent with adenocarcinoma. Gram staining revealed no organisms. Intravenous contrast-enhanced CT of the abdomen showed a large amount of ascites and a new low-density area in the portal vein suggestive of a portal thrombus (Fig. 1). Empiric antimicrobial therapy with intravenous piperacillin/tazobactam and oral edoxaban were initiated. The patient's symptoms subsided shortly, and his ascitic fluid, blood, and urine cultures remained negative. Antibiotic therapy was terminated 3 days later, and the patient was discharged. He resumed the second course of chemotherapy at our outpatient clinic 4 days later but developed a fever

☆ All authors meet the ICMJE authorship criteria.

* Corresponding author. Department of Infectious Diseases, University of Tokyo Hospital, Hongo 7-3-1, Bunkyo-ku, Tokyo, 113-8655, Japan.
E-mail address: kokamoto-tky@umin.ac.jp (K. Okamoto).

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Table 1
Results of ascitic fluid analysis.

	3 weeks prior	On admission	Hospital day 8	Hospital day 12
White blood cell counts (/μL)	700	3900	500	500
Polymorphonuclear cells (/μL)	119	2535	60	15
Albumin (g/dL)	2.0	2.0	1.3	1.3
Serum ascites albumin gradient (g/dL)	0.8	0.7	Not obtained	0.7
Total protein (g/dL)	3.7	3.8	3.1	3.4
Lactate dehydrogenase (U/L)	209	247	228	184
Amylase (U/L) (normally half of serum concentration)	Not obtained	Not obtained	Not obtained	585
Glucose (mg/dL) (normally same as serum concentration)	Not obtained	Not obtained	Not obtained	157
Culture	No growth	*Aeromonas hydrophila*, *Escherichia coli*	Not obtained	No growth

and abdominal bloating 2 weeks after discharge and presented to our hospital.

Upon arrival at our hospital, he was alert and oriented and was not in acute distress. His vital signs were as follows: body temperature, 37.8 °C; pulse rate, 113 beats per minute; blood pressure, 120/62 mmHg; respiratory rate, 12 breathes per minute; and oxygen saturation, 94% while breathing ambient air. His abdomen was severely distended and tender with guarding. There were no skin stigmata suggestive of cirrhosis or portal hypertension (i.e. caput medusae). The following blood test results were remarkable: an elevated white blood cell count of 13,700/μL and C-reactive protein level of 19.6 mg/dL (reference, 0–0.3 mg/dL). His liver enzyme levels remained mostly unchanged since the time of pancreatic cancer diagnosis, with normal levels of aspartic and alanine aminotransferase, a total bilirubin level of 1.2 mg/dL, gamma-glutamyltransferase level of 554 IU/L, and alkaline phosphatase level of 1116 U/L. An ascitic fluid analysis revealed elevated albumin and lactate dehydrogenase (LDH) levels and an increased white blood cell count (Table 1). CT of the abdomen revealed no changes in the liver metastases, peritoneal carcinomatosis, and ascites. The portal thrombus had decreased in size, and the intestinal wall was edematous. No findings indicated visceral perforation or infection.

At this time, empirical piperacillin/tazobactam therapy was initiated. After a 3-day incubation, 2 g-negative bacilli, identified as *Aeromonas hydrophilia* and *Escherichia coli* using matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI Biotyper 3.1, Bruker Daltonics, the United States) grew in ascitic fluid culture. *A. hydrophila* was susceptible to piperacillin/tazobactam, ceftriaxone, meropenem, aztreonam, and levofloxacin, while *E. coli* was pan-susceptible. The blood cultures remained negative. Piperacillin/tazobactam therapy was continued, and a percutaneous tube was placed in the peritoneum for symptomatic control on hospital day 5. The patient's ascitic fluids were repeatedly sent for analysis (Table 1). After treatment, his fever subsided and abdominal bloating improved greatly, with a decrease in the number of polymorphonuclear cells in the ascites.

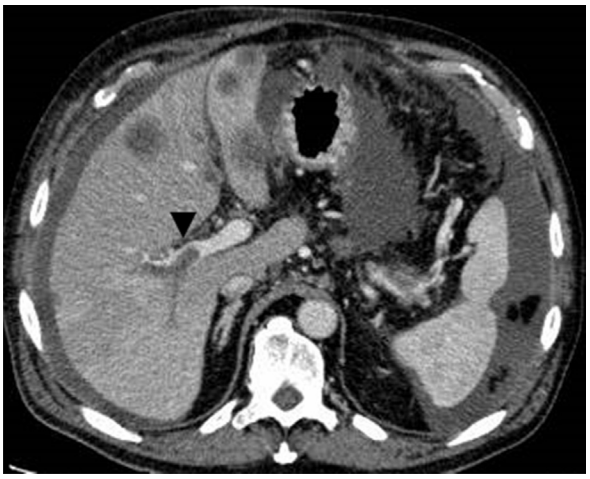

Fig. 1. Intravenous contrast-enhanced computed tomography of the abdomen at the time of diagnosis of metastatic pancreatic cancer (transverse view). A new low-density area in the portal vein is suggestive of a portal thrombus (black arrowhead).

Despite these improvements, his hospital course was complicated by development of a pancreatic pseudocyst with fistula and small bowel obstruction, most likely caused by the pancreatic carcinoma. His condition deteriorated despite invasive measures and he expired on hospital day 32 after a transition to comfort care.

3. Discussion

Two main types of bacterial peritonitis have been identified, and are defined by the presence or absence of a surgically correctable lesion in the abdominal cavity [2]. SBP occurs in the absence of an intra-abdominal infectious source, and virtually all cases of SBP develop in patients with cirrhosis [1], a condition that reduces small bowel motility and causes bacterial translocation of the intestinal tract [3,4]. Here, portal hypertension increases the likelihood of a mesenteric lymphatic rupture, which can provide a bacterial entry site [5]. Cirrhosis-related ascites contains a relatively smaller concentrations of immune-related proteins (e.g., complement, immunoglobulin) and is therefore more susceptible to infection [6]. Moreover, cirrhotic patients also exhibit reduced phagocytic activity in the hepatic reticuloendothelial system and are thus vulnerable to bacteremia [7]. All these factors are thought to contribute to the development of SBP.

By contrast, secondary bacterial peritonitis is caused by the direct dissemination of bacteria from a surgically treatable lesion or focal infection into an abdominal cavity. Although an apparent source of bacterial dissipation can lead to an immediate diagnosis, not all cases present with an easily visible bacterial entrance. According to previous reports, an elevated total protein (>1 g/dL), decreased glucose (<50 mg/dL), elevated LDH level (greater than the upper limit or serum concentration) and polymicrobial ascitic infection are features suggestive of secondary bacterial peritonitis [8]. An inadequate response to optimal antibiotic therapy may also suggest a secondary etiology [2].

Our patient exhibited elevated ascitic protein and LDH levels, a low serum ascites albumin gradient, and polymicrobial infection but responded well to antibiotic monotherapy. We therefore suspected spontaneous bacterial peritonitis of the malignant ascites, as his peritoneal organs were intact and he responded well to medical therapy alone in the absence of cirrhosis. Consistent with previous reports [9,10], the liver metastases and portal vein thrombosis observed in this case may have predisposed the patient to SBP. This condition may also have context of intestinal edema from malignant ascites. Alternatively, however, this condition may have developed secondarily to a radiographically unapparent leakage

Table 2
Previously reported cases of bacterial peritonitis in patients with malignant ascites.

Case	Age/Sex	Type of cancer	Causative organism	Suspected etiology	Reference
1	61/female	Ovarian cancer	*Bacteroides* spp	Accidental intestinal aspiration	[14]
2	87/female	Unknown (adenocarcinoma)	*Escherichi. coli*	Indwelling catheter	[14]
3	24/male	Unknown (adenocarcinoma)	*E. coli*	Generalized sepsis	[14]
4	64/female	Gastric cancer	*Streptococcus pneumoniae*	Massive liver metastasis	[9]
5	42/male	Gastric cancer	*Enterobacter aerogenes*	Bowel ischemia caused by hypotension	[15]
6	28/female	Gastric cancer	*Salmonella arizonae*	High virulence of *Salmonella* spp.	[13]
7	unknown	Peritoneal adenocarcinoma	*Klebsiella pneumoniae*	Portal vein thrombosis	[10]
8	unknown	Unknown (adenocarcinoma)	*E. coli*	Liver metastasis	[10]
9	64/male	Pancreatic cancer	*Aeromonas hydrophilia*	Liver metastasis	This case
			E. coli	Portal thrombosis	

from a visceral organ, as indicated by polymicrobial peritonitis with elevated protein and LDH levels in the ascites. However, the patient's protein and LDH levels were elevated even before the confirmation of bacterial peritonitis, most likely due to carcinomatosis peritoneum. Some might argue that bacterial peritonitis might have been related to endoscopic ultrasound fine needle aspiration the patient underwent about a month prior. However, this is felt to be very unlikely because of 1) the long interval between the procedure and the development of bacterial peritonitis without other signs or evidence of complications such as pancreatitis and 2) the proximity of pancreas head and duodenal wall in contrast to the distance between pancreas body/tail and gastric wall.

Despite the large number of patients with malignant ascites, few cases of bacterial peritonitis in malignant ascites have been reported (Table 2). One possible explanation is the high protein concentration in malignant ascites. Previous reports indicate that spontaneous bacterial peritonitis normally occurs in ascitic fluid with a low protein concentration, which is associated with low opsonic activity and a low concentration of the complement factors C3 and C4 [11,12]. Malignant ascites contains a relatively high protein level, which facilitates resistance to infectious bacteria, excepting organisms such as *Salmonella* [13].

Kurtz et al. reviewed 101 patients with malignant ascites and found that only three yielded positive ascitic fluid cultures [14]. All three patients had other predisposing factors for bacterial peritonitis, such as intestinal perforation, indwelling peritoneal catheters, and generalized bacteremia, suggesting the likelihood of a secondary etiology. To date, three cases of bacterial peritonitis have been associated with gastric cancer. In one case, the patient presented with *Streptococcus pneumoniae* peritonitis associated with a massive hepatic metastasis [9], and the author attributed this infection to a reduction in hepatic bacterial filtration. A second case involved *Enterobacter aerogenes* peritonitis in a patient experiencing frequent episodes of hematemesis [15], and the author suspected that the resulting hypotension led to bowel ischemia, which altered the permeability of intestinal wall and caused bacterial translocation. In a third case reported by Woolf et al., a patient with gastric cancer and peritoneal carcinomatosis developed *Salmonella arizonae* peritonitis [13], and the authors attributed this infection to the highly virulent bacterial pathogen. Another group of authors reported *Klebsiella pneumoniae* peritonitis in a patient with peritoneal adenocarcinoma and portal vein thrombosis [10] and hypothesized that portal hypertension led to bacterial peritonitis. Therefore, our report is the first to describe a case of bacterial peritonitis in malignant ascites from pancreatic cancer.

Aeromonas spp. are gram-negative rod bacteria that exist in a wide range of fresh water and marine environments. Although *Aeromonas* spp. are a relatively less frequent cause of peritonitis, compared to other enteric bacteria such as *E. coli* and *Klebsiella* spp., these bacteria have been reported as a cause of SBP, particularly in East Asia during warmer months [16], as well as of secondary bacterial peritonitis [17]. Notably, the mortality and morbidity attributed to *Aeromonas*-associated SBP are similar to those attributed to other pathogens [16].

In conclusion, we present here a case of bacterial peritonitis caused by *A. hydrophila* and *E. coli* in a patient with metastatic pancreatic carcinoma who presented no clear evidence indicative of secondary peritonitis. Although bacterial peritonitis rarely develops in malignant ascites, in contrast to cirrhotic ascites, bacterial peritonitis is a medically treatable disease, even in the absence of cirrhosis or evidence of visceral fluid leakage into the peritoneum. Our case highlights the importance of thorough evaluation of ascites with biochemical, microbiological, and cytological examinations.

Conflicts of interest

None declared.

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