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Case Report

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Spontaneous Bacterial Empyema Caused by *Haemophilus influenzae* in a Patient with Decompensated Alcoholic Liver Cirrhosis

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Abstract

Introduction: Spontaneous bacterial empyema (SBEM) is an infection of a preexisting hydrothorax in patients with cirrhosis. *Haemophilus influenzae (H. influenzae)* is a Gram-negative bacteria that is commonly involved in upper and lower respiratory infections. Herein, we report our experience with SBEM in a patient with decompensated alcoholic liver cirrhosis caused by *H. influenzae*.

Case presentation: A 63-year-old man with alcoholic decompensated liver cirrhosis, Child-Pugh class C, and a Model for End-Stage Liver Disease score of 21, was admitted to our hospital. On admission day (day 1), the patient had jaundice with icteric conjunctiva, decreased lung sounds in entire right side of the chest. On the next day (day 2), the patient had fever of 39.2°C. A Gram stain of the pleural effusion revealed Gram-negative rods with remarkable leukocytosis. The blood and pleural effusion cultures were both positive for beta-lactamase-negative ampicillin-resistant *H. influenzae*. In spite of intensive care for septic shock, his comatose status and liver failure had not improved, and on day 21, the patient died of multiorgan failure.

Conclusion: Although *H. influenzae* is thought to be an indigenous microorganism in the respiratory tract, to our knowledge, there are no case reports of *H. influenzae* as a causative bacterium of SBEM. Our case suggests that it is essential to investigate the pathogenesis of hepatic hydrothorax in patients with cirrhosis as well as to offer systemic management and care for bacterial infections.

Keywords

Cirrhosis; Alcoholic liver disease; Hydrothorax; Empyema

Introduction

Late-stage liver cirrhosis often leads to peritoneal effusion and hepatic hydrothorax in some cases. Infection of the peritoneal effusion and hydrothorax lead to a critical condition in patients with liver cirrhosis. Spontaneous bacterial empyema (SBEM) is an infection of a preexisting hydrothorax in patients with cirrhosis and is reported to occur in 13% of such cases [1]. Clinical studies demonstrate a close relationship between the causative organisms of SBEM and spontaneous bacterial peritonitis (SBP). The major pathogenic bacteria in SBEM and SBP are aerobic Gram-negative bacilli, such as *Escherichia coli* and *Klebsiella pneumoniae* as well as aerobic Gram-positive cocci, such as *Staphylococcus aureus* and *Enterococcus* species [2]. *Haemophilus influenzae (H. influenzae)*, belonging to the *Pasteurellaceae* family, is a Gram-negative bacteria that is commonly involved in upper and lower respiratory infections. However, SBP caused by *H. influenzae* is rare with few cases reported [3,4]. It is largely unknown whether *H. influenzae* causes SBEM. Herein, we report our experience with SBEM in a patient with decompensated alcoholic liver cirrhosis caused by *H. influenzae*.

Case Report

A 63-year-old man with alcoholic decompensated liver cirrhosis, Child-Pugh class C, and a Model for End-Stage Liver Disease score of 21, was admitted to our hospital. He had been drinking alcohol, approximately 1100 mL of distilled spirits (equal to 200 g ethanol) per day, for over 30 years. Seventeen months prior to hospitalization, the patient presented to a community hospital complaining of swelling in both lower legs. He had been treated several times for severe hepatic hydrothorax. On admission day (day 1), the patient had jaundice with icteric conjunctiva, decreased lung sounds in entire right side of the chest, and pitting edema in the bilateral lower legs without any sign of encephalopathy. Laboratory evaluation was notable for anemia with hemoglobin 12.7 g/dL, thrombocytopenia 58,000/mm^3, prothrombin time-international normalized ratio 1.94, total protein 6.5 g/dL, albumin 1.6 g/dL, total bilirubin 5.6 mg/dL, aspartate aminotransferase 47 IU/L, alanine aminotransferase 23 IU/L, and alkaline phosphatase 506 IU/L (Table 1). Further evaluation revealed a negative viral hepatitis panel and autoimmune panel. Viral infections such as CMV, HTLV-1, and HIV were ruled out. Initial infectious work-up with a throat swab, urine sample, and stool sample was negative. X-ray examination showed a remarkable right-sided hydrothorax. Abdominal contrast enhanced computed tomography (CT) demonstrated a cirrhotic liver with minimal ascites (Figure 1). On the next day (day 2), the patient had fever of 39.2°C. Blood cultures were performed, and ceftriaxone was administered as empiric therapy. He developed hypoxemia on day 2, and 900 mL of pleural fluid was aspirated. A Gram stain of the pleural effusion revealed Gram-negative rods with remarkable leukocytosis (23200/μL, with segmented neutrophils of 95%), and the antibiotics were switched to ampicillin-sulbactam. In spite of the thoracentesis, on day 4, his dyspnea still remained, his tachypnea was aggravated, and his blood pressure had decreased. He was diagnosed with septic shock, and he was treated with meropenem, ciprofloxacin, catecholamines, and continuous hemodiafiltration in the intensive care unit. Hydrocortisone was also administered because of adrenal crisis. A catheter was placed in the right hemithorax for continuous drainage. There was not enough ascites detected by abdominal sonography to perform abdominocentesis. The blood and pleural effusion cultures were both positive for beta-lactamase-negative ampicillin-resistant *H. influenzae*, for which meropenem and ciprofloxacin were administered. On day 8, chest CT detected pleural fluid with hematoma in the right lower hemithorax. Thoracoscopic debridement and pleural irrigation were performed. After the surgery, the sedative drug was discontinued, but his comatose status persisted. Head CT

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Table 1: Laboratory evaluation.

Hematology		Blood chemistry		
WBC	8300/μl	TP	6.5	g/dl
Neutrophils	78%	ALB	1.6	g/dl
Eosinophils	8%	T.bil	5.6	mg/dl
Lymphocytes	9%	AST	47	IU/l
RBC	365/μl	ALT	23	IU/l
Hemoglobin	12.7 g/dl	GGT	43	IU/l
Hematocrit	36.8%	ALP	506	IU/l
Platelets	58000/μl	LDH	238	IU/l
Coagulation		ChE	63	IU/l
PT	37%	Na	139	mEq/l
PT-INR	1.94	K	4.1	mEq/l
APTT	70.3 s	Cl	103	mEq/l
Viral marker		BUN	19	mg/dl
HBsAg	(-)	Cre	1.12	mg/dl
HBsAb	(-)	NH3	59	μg/dl
HBcAb	(-)	Type 4 collagen	344	ng/ml
HCVAb	(-)	Hyaluronic acid	3920	ng/ml
HIVAb	(-)	HGF	0.74	ng/ml
Tumor marker		β-D glucan	8.4	pg/ml
AFP	3.2 ng/ml	CRP	0.71	mg/dl
DCP	1367 mAU/ml			

WBC: White Blood Cell Count; RBC: Red Blood Cell Count; PT: Prothrombin Time; INR: International Normalization Ratio; APTT: Activated Partial Thromboplastin Time; HBsAg: Hepatitis B Surface Antigen; HBsAb: Hepatitis B Surface Antibody; HBcAb: Hepatitis B Core Antibody; HCVAb: Hepatitis C Virus Antibody; AFP: Alpha-Fetoprotein; DCP: Des-gamma-carboxy Prothrombin; TP: Total Protein; ALB: Albumin; T.bil: Total Bilirubin; AST: Aspartate Transaminase; ALT: Alanine Transaminase; GGT: gamma-Glutamyl Transpeptidase; ALP: Alkaline Phosphatase; LDH: Lactate Dehydrogenase; ChE: Cholinesterase; Na: Sodium; K: Potassium; Cl: Chloride; BUN: Blood Urea Nitrogen; Cre: Creatinine; NH3: Ammonia; HGF: Hepatocyte Growth Factor; CRP: C-Reactive Protein.

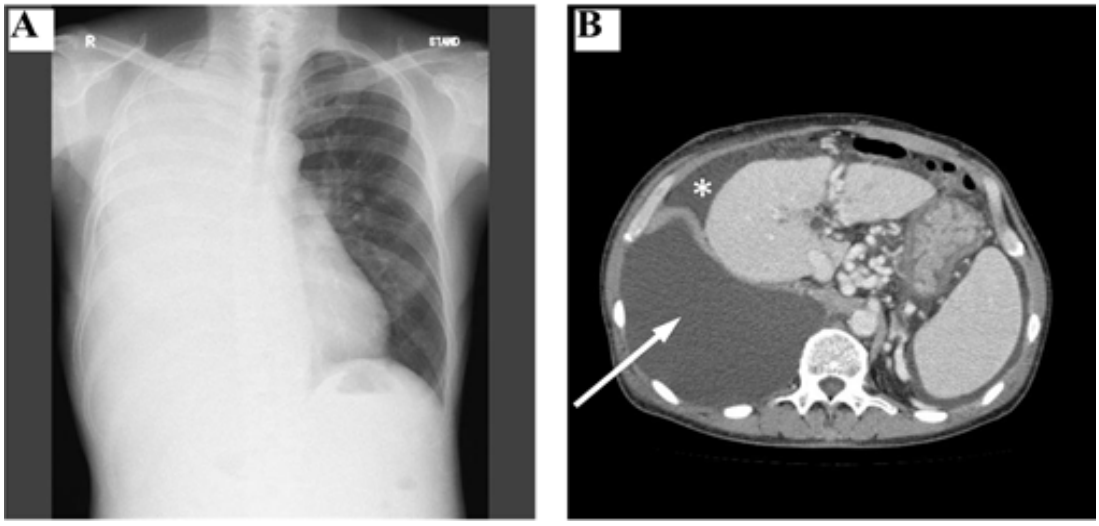

Figure 1: A. Chest X-ray taken on the day of admission showing significant right-sided hydrothorax. B. Abdominal contrast-enhanced computed tomography taken 27 days before admission showing hydrothorax (→) and a small amount of ascites (*).

and magnetic resonance imaging revealed no significant intracranial hemorrhage or cerebral edema. In spite of intensive care for septic shock, his comatose status and liver failure had not improved, and on day 21, the patient died of multiorgan failure.

Discussion

Hepatic hydrothorax is defined as the presence of pleural fluid (usually greater than 500 mL) in a patient with cirrhosis in the absence of primary cardiac or pulmonary disease [5-7]. Hepatic hydrothorax occurs approximately 6–13% of patients with advanced cirrhosis and is often associated with alcoholic liver cirrhosis [8-10]. Patients with cirrhosis and hepatic hydrothorax are prone to spontaneous infection of pleural fluid [1,11]. In general, cirrhosis is an immunocompromised state that increases a patient's susceptibility to the development of spontaneous bacterial infections and a variety of infections from uncommon pathogens [12,13]. SBEM is defined as infection of a preexisting hydrothorax in a patient with cirrhosis [1,11]. A diagnosis of SBEM is established if the pleural fluid cultures are positive and

a polymorphonuclear count is >250 cells/μL. The patient in this case report met both these criteria [11]. Low pleural fluid opsonic activity and C3 levels are found in patients with cirrhosis, who are at high risk of SBEM [14]. In our case, the route of *H. influenzae* to the pleural fluid was uncertain; it was not clear whether it was from the respiratory tract or the gastrointestinal tract. Regarding liver cirrhosis, the major causative organisms of all bacterial infections are Gram-negative bacteria, while Gram-positive bacteria comprise about 20% and anaerobic bacteria only 3% [12]. A recent study reveals that Gram-positive cocci such as *Staphylococcus*, *Enterococcus,* and multi-resistant bacteria have become common pathogens [15]. Therefore, the etiology of bacterial infections in liver cirrhosis can be not only gastrointestinal tract sources but could also arise from other organs. The pathogenesis of SBEM, SBP, and spontaneous bacteremia is considered to be similar; they share the same types of common pathogens [16]. In our case, we could not rule out complications of SBP, as the patient's ascites was too small to evaluate. However, SBEM can occur either with SBP (transdiaphragmatic spread) or without SBP (hematogenous spread) [16]. Therefore, it might be possible that bacteremia by *H. influenzae* results in SBEM. In previous reports, major causative microorganisms of SBEM were *E. coli*, *Streptococcus* species, *Enterococcus* species, and *Klebsiella* pneumonia [1,11]. These bacteria have been thought to originate from the gastrointestinal tract or to be systemic in origin [3]. Although *H. influenzae* is thought to be an indigenous microorganism in the respiratory tract, to our knowledge, there are no case reports of *H. influenzae* as a causative bacterium of SBEM [3]. Several reports reveal that *H. influenzae* is an indigenous bacterium in the human gastrointestinal tract [17-19]. This fact might support that SBEM in this case occurred by the same pathway as the other major SBEM source. SBEM without ascites has been previously reported, and the pathogenic bacteria were *E. coli*, *Pseudomonas stutzeri,* and *Enterococcus faecium* [1]. If we take into account that *H. influenzae* is an indigenous bacterium of the intraperitoneal cavity, our case may support the hypothesis that enteric microorganisms reach the pleural fluid through bacteremia [1]. SBEM has a high recurrence rate (25-30%) and a poor prognosis [1]. For example, Xiol et al. reported that SBEM was fatal in 6 out of 16 cases [10]. Although SBEM is a rare common complication of liver cirrhosis, physicians should consider not only spontaneous bacterial peritonitis but also SBEM when a patient with cirrhosis and hydrothorax presents with infective symptoms such as fever and dyspnea. Moreover, these patients need to be intensively cared for because of their impaired immune systems, as they can very easily develop septic shock. In conclusion, we encountered a rare case of SBEM caused by *H. influenzae*. Our case suggests that it is essential to investigate the pathogenesis of hepatic hydrothorax in patients with cirrhosis as well as to offer systemic management and care for bacterial infections.

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