Spontaneous Peritonitis of Liver Cirrhosis
— An Autopsy Case —

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Summary: A 27-year-old man with decompensated liver cirrhosis developed clinical characteristics of peritonitis, i.e. abrupt onset of fever, chills, abdominal pain with rebound tenderness and absent bowel sound, hypotension and leukocytosis. The patient expired despite vigorous antibiotic interfusion. An autopsy showed liver cirrhosis, splenomegaly and localized colitis. It was our speculation that weakened local resistance of the intestinal mucosa due to colitis may have led to the invasion of the peritoneal cavity by the enteric bacteria, *serratia marcescens*.

Keywords: *serratia marcescens* — liver cirrhosis — spontaneous peritonitis — Kupffer cell — bacterascites

Introduction

Spontaneous bacterial peritonitis is one of the complications of advanced cirrhosis of the liver. This was first reported about 90 years ago by Charrin and Veillon (1893), and has recently gained recognition for its clinical importance. In this paper we describe a rare case of liver cirrhosis and peritonitis due to *serratia marcescens*.

Case Report

This was the fifth admission for this 27-year-old carpenter whose chief complaint was drowsiness. At age 20, this patient was hospitalized because of acute hepatitis, and at age 23, he was again hospitalized because of chronic hepatitis.

Eleven months prior to admission, he visited Inagi City Hospital, Tokyo, because of jaundice and abdominal distention. He returned to Hita, Ooita, and was hospitalized at Iwao Hospital for 5 months. A diagnosis of liver cirrhosis was established by liver function tests, scintigrams of the liver and the spleen, and physical findings. Liver biopsy was not done. After his leaving against medical advice, hyperbilirubinemia had persisted. Three months later, he was readmitted to Iwao Hospital because of fever, jaundice and abdominal pain. A diagnosis of appendicitis was made at another hospital and antibiotics had been given. On the 12th hospital day, he became unresponsive. On the 14th day, he was transferred to Kurume University Hospital.

He had history of smoking and drinking. Serologic tests for HBsAg of his father and siblings were positive.

Physical Examination: The body temperature 37.1°C, the pulse 90/min regular,
the respiration 20/min, the blood pressure 108/50 mmHg. The skin was deeply icteric and demonstrated numerous petechiae and spider angiomata. There was no lymph node enlargement. The bulbar conjunctivae were icteric and the palpebral conjunctivae were anemic. The pharynx was slightly reddened. The thyroid was not palpable. Gynecomastia was present. The cardiac dullness was not enlarged. Heart murmurs were not audible. The peripheral pulses were full and equal. There was edema of the legs. The liver was not palpable and the upper level of the liver dullness was unclear. The abdomen was distended and tympanitic, and fluid wave was noted. The bowel sounds were hypoactive. He was drowsy. The cranial nerves were intact and Babinski reflexes were negative.

Laboratory Data: The hemoglobin 8.3 g/dl, the hematocrit 26%, the erythrocyte count $246 \times 10^4$, the leukocyte count 18,200 (stab 17%, seg 78%, lym 4% and mon 1%). The bleeding time was 6'00" (control: 2'-3''), and the coagulation time was 17'00" (control: 5''-15''). The blood glucose was 68 mg/dl, the urea nitrogen 43.5 mg/dl, the creatinine 1.4 mg/dl, total bilirubin 16.4 mg/dl, direct bilirubin 8.1 mg/dl, total protein 4.2 g/dl (albumin 46.5%, γ-Globulin 37.8%) and ammonia 42 μg/dl. The sodium was 117 mEq/L, the potassium 4.1 mEq/L, the chloride 90 mEq/L, and the calcium 7.6 mg/dl. The prothrombin time was 21.6" (13"-18''), GOT 142 IU, GPT 42 IU, Al-p 13.2 KAU, LDH 429 IU, ZTT 8.4 KU, TTT 6.1 KU. Serologic testing showed (+) HBsAg, (-) HBeAg and (+) anti HBe.

On the evening of the 1st hospital day, blood pressure dropped suddenly to 64/20 mmHg. Oliguria was noted. The abdominal wall of entire right side was rigid, and marked tenderness was present at McBurney's point and Lanz's point. Rebound tenderness was present. Acute appendicitis with localized peritonitis and paralytic ileus were considered. Antibiotics (cephazolin 2 g/day) were given. He passed tarry stool and diarrhea. Next morning the blood pressure again dropped suddenly to 70-40 systolic. The leukocyte count was 18,000, with a slight left shift. Abdominal paracentesis revealed cloudy ascitic fluid with a specific gravity of 1.010; culture eventually grew out *serratia marcescens*. The clinical signs of peritonitis did not subside. The patient expired in spite of vigorous antibiotics treatment. An autopsy was performed.

**Autopsy Findings**

Gross Findings: The body was that of a well-built young adult male weighing 58 kg and measuring 160 cm in height. The skin was icteric. There was no palpable lymph node in the cervical, axillary or inguinal regions. The abdomen was slightly distended with fluctuation. Both lungs were collapsed and inflated, in part. The right pleural effusion measured 600 ml and the left 7 ml. There was no fibrous pleural adhesion. The peritoneal cavity contained a small amount of turbid, yellowish fluid and a yellowish-white pus in the rectovesical excavation. The liver (700 g) was firm and the surface was coarsely nodular. The cut surface showed round to oval nodules of dark green parenchyma, separated by dark red fibrous bands of varying thickness (Fig. 1 and 2). The presence of marked jaundice in pseudolobules gave the liver a dark green appearance. The bilateral hepatic ducts and the common bile duct were not obstructed. Lymph nodes were enlarged in the hepatic portal, the head of the pancreas and around the abdominal aorta. The spleen (440 g) showed marked congestion and the follicles were not prominent. The gastrointestinal tract, especially small intestine and large intestine, were edematous. Varicose veins in the submucosa of the esophagus were not seen. The gastric mucosa was edema-
Fig. 1, 2. Macronodular cirrhosis. Cut-surface of the liver showing round to oval nodules separated by fibrous bands.

Fig. 3. The serosa of the ascending colon, appearing markedly dark red and without adhesions to other organs.

Fig. 4. Histological appearance of the liver, showing a disruptive lobular architecture. Nodules are infiltrated with inflammatory cells. There is evidence of bile duct proliferation at the periphery of the nodules. H and E. ×40.

tous, erythematous and covered with mucus. There were hemorrhagic spots and small erosions with well-defined edges and a greish base. Petechial hemorrhage or mucosal bleeding with tarry contents were present. Small parts of the mucosa and the serosa of the cecum and ascending colon were markedly dark red and without adhesions to other organs (Fig. 3). The kidneys (right: 250g, left: 230g) were markedly swollen and stained yellowish brown. The pancreas was firm and deep brown in color. The heart (270g) was unremarkable. The major blood vessels showed no demonstrable abnormalities.

Microscopic findings: The liver showed complete cirrhotic change (Fig. 4). The normal lobular architecture was distorted. Irregular fibrous bands were seen, containing lymphoid infiltrates, erythrocytes and proliferation of the bile ducts with bile stained material within the lumen. Cholestasis was seen at the periphery of the regenerative nodules. Kupffer cells showed cytoplasmic bile staining.

The villi of the ascending colon were not flat nor atrophic, and crypts were not destroyed. Some inflammatory infiltrates were present in the lamina propria and the submucosa. Heavy infiltrates of polymorphonuclear leukocytes and bacteria were seen in the serosa (Fig. 5).
Fig. 5. Histological appearance of the serosa, taken from the ascending colon. Note the heavy infiltrates of polymorphs and bacteria. H and E. ×40.

Bile stained casts were seen in the lumen of the tubules of the kidneys. Interstitial edema and lymphoid infiltrates were seen in the subcapsular area.

Venous sinuses of the spleen were markedly dilated and filled with erythrocytes. Atrophy of lymphoid tissue was noted.

The lymph nodes of the hepatic portal, the pancreatic head, and around the abdominal aorta showed sinus histiocytosis and/or reactive hyperplasia.

Discussion

Spontaneous peritonitis of liver cirrhosis was re-evaluated by Caroli and Platteborse (Caroli and Platteborse, 1958) and Conn (Conn, 1964). This is characterized by sudden fever, leukocytosis, shaking chills, diffuse abdominal pain, non-localizing rebound tenderness, hypoactive bowel sounds, hypotension, hepatic coma and turbid ascitic fluid with a specific gravity of approximately 1.013. The pathogenesis was studied by Conn (Conn, 1964; Conn, 1975). He stated that bacteria might initially penetrate the intestinal mucosa and escape the blood flow and/or lymphatics and the peritoneal cavity, and that impairment of phagocytic activity of the liver might not preclude the formation of secondary bacteremia.

In general, patients with cirrhosis have an increased susceptibility to infections. Those responses include the failure of Kupffer cells (Bjørneboe and Prytz, 1975; Kurahori et al, 1979), the impaired leukocytes chemotaxis (Maderazo, Ward and Quintiliani, 1975) and the accumulation of ascitic fluid in which the bacteria can multiply.

The Kupffer cells of the normal liver play an important role in removing micro-organisms in the portal blood, in inactivating endotoxin (Bradfield, 1974), and in clearing macromolecules or immune complexes (Liehr, 1978). In advanced cirrhosis of the liver, the blood flow may be altered in such a way that some of the portal blood bypasses the liver, because of the development of intrahepatic and extrahepatic portal systemic shunts. Most of the circulating bacteria may not pass through the hepatic reticuloendothelial filter. The portal systemic shunt may be responsible for the great reduction of hepatic clearance of ammonia and other toxins. Since bile pigments were ingested by Kupffer cells in our case, Kupffer cells' phagocytic activity per se appeared minimally affected. On liver scintigram, the liver showed diminished uptake of radioisotopes ingested by Kupffer cells and was atrophic in size. Shunting of blood away from the hepatic sinusoids allows particles normally taken up by Kupffer cells to enter the systemic circulation, and the function of Kupffer cells themselves may be abnormal, as demonstrated in some patients with alcoholic cirrhosis (Cookson, Powell and Halliday, 1973), and in about half of the patients with cholestasis or obstructive jaundice (Drivas, James and Warble, 1976). Although blood culture was not done, poor perfusion of the blood and damage of the Kupffer cells by hepatitic virus and alcohol might have reduced the hepatic filtering activity of the microorganisms.
In our case, a culture of ascitic fluid grew *serratia marcescens* conforming to the definition of the enteric bacteria, although blood culture was not done. Spontaneous peritonitis due to *serratia marcescens* in a patient with liver cirrhosis is rare (Conn, 1964; Hasumura, Takata and Takada, 1972; Mukuda et al., 1978). *Serratia marcescens* is a small, motile, Gram-negative rod and a facultative anaerobe. Pigmented and non-pigmented strain are found in the human respiratory tract and in feces. On the surface of the intestinal lumen, the organisms generally do not represent a diseased condition and may even, as other enteric bacteria, contribute to normal function and nutrition. They become pathologic only when they infiltrate tissue outside the intestinal tract, the urinary tract, the biliary tract, the lung, the peritoneum or the meninges. *Serratia*, usually non-pigmented strains, may cause pneumonia and iatrogenic sepsis as an opportunistic pathogen in hospitalized patients. Endotoxin shock is a very serious complication of Gram-negative enteric bacteria including *serratia marcescens* (Wilson and Miles, 1975).

Bacterascites may be classified into two groups, aerobic and anaerobic. Some authors studied clinically and experimentally spontaneous bacterial peritonitis due to anaerobes and reported interesting results. According to Targan et al (Targan et al., 1977), who reviewed a total of 126 cases of peritonitis of liver cirrhosis, bacterascites due to anaerobic or microaerophilic bacteria was seen in 8 cases (6%). Concurrent bacteremia was seen in only one of 8 cases. Bacterascites due to aerobic bacteria was noted in 118 cases (94%) of spontaneous peritonitis and concurrent bacteremia occurred in 52 (44%) of 118 cases. It was stressed that the incidence of spontaneous peritonitis due to anaerobic or microaerophilic bacteria was relatively low despite the high density of these organisms in the normal flora. The escape of bacteria from the intestinal tract resulted primarily in contamination of the peritoneal cavity and secondarily in bacteremia.

On the other hand, according to the experiments by Onderdonk et al (Onderdonk et al., 1976), intraabdominal abscess was one of the characteristic features in the late phase of anaerobic or microaerophilic peritonitis. It seemed to result from a mixed infection disclosed that aerobacteria were predominant and invasive in the early stage and that the peritonitis might progress to intraabdominal abscess in which anaerobes predominated in the late stage.

Although existence of free air in the abdominal cavity was not clinically ascertained, no perforation of the gastrointestinal tract was found on gross examination at autopsy. The lesion of the ascending colon showed microscopic edema, hyperemia, intense polymorphonuclear infiltration and many bacteria in the colonic wall. There is no doubt that this lesion was the source of the infection. The transmural migration of intestinal bacteria might account for contamination of ascites without requiring a preliminary spontaneous bacteremia. In fact, Kerr, Pearson and Read (Kerr, Pearson and Read, 1963) and Conn (Conn, 1964) reported cases without positive blood cultures.

In our case, although certain predisposing factors such as catheterization for angiography, portocaval or splenorenal shunt operation, small bowel biopsy and ulcerative lesions of the gastrointestinal tract were absent, other possible factors, i.e. administration of antibiotics, melena due to gastric erosion and diarrhea, are noted. Antibiotics may alter the bacterial intestinal flora and may permit overgrowth of the strain of bacteria that otherwise would not be particularly invasive or virulent to the patient. Diarrhea may also cause alteration in both the types of bacteria and in the physical distribution of...
flora in the intestinal tract. These considerations may play a part in altering the permeability of the mucosal barrier and enabling the bacteria to invade the peritoneal cavity through the intestinal mucosa without prior bacteremia (Schweinberg, Seligman and Fine, 1950). Conn speculated that hypoalbuminemia and an elevated blood urea nitrogen level may also predispose a patient to such a process.

In an autopsy series of the Pathology Department, Kurume University, the increase in the number of cases associated with *serratia* infection is speculated to be associated with the increasing use of antibiotics. With the introduction of penicillin for clinical use, the incidence of infection in cirrhosis, including bacterial peritonitis, has decreased (Davidson, 1970). *Serratia marcescens* is nearly always highly resistant to cephalosporin and polymyxin B, but it is less often resistant to ampicillin (Wilson and Miles, 1975). *Serratia* infection can be prevented by selection of appropriate antibiotics for treatment. Indeed, peculiar complications such as spontaneous peritonitis may be rare, but every effort should be made to rule out the diagnosis. Spontaneous peritonitis can be treated with the appropriate antibiotics.

With our case study, we would call attention to the possibility of the development of spontaneous peritonitis in the presence of liver cirrhosis, the necessity of its early diagnosis and the clinical significance of prophylactic procedures.

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