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## Abstract

Clostridium perfringens infection is a very rare cause of massive intravascular hemolysis, but it should always be kept in mind, since only early treatment can rescue patients from an otherwise rapidly fatal outcome. We report a case of a 78-year-old diabetic male who was admitted complaining of general fatigue, dark red urine, and vomiting. His blood revealed massive hemolysis. Computer tomography demonstrated huge liver abscess in the right lobe of the liver. About 1 h after admission, he suddenly fell into a critical condition. He died 3 h after admission in spite of intensive care and resuscitation. Clostridium perfringens was detected from the blood taken before death and from liver abscess by biopsy after death. We concluded that this patient died of acute massive intravascular hemolysis in septicemia caused by Clostridium perfringens infection.

**KEYWORDS:** Clostridium perfringens, intravascular hemolysis, liver abscess

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*Case Report*

# Massive Intravascular Hemolysis in a Patient Infected by *Clostridium perfringens*

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***Clostridium perfringens*** **infection is a very rare cause of massive intravascular hemolysis, but it should always be kept in mind, since only early treatment can rescue patients from an otherwise rapidly fatal outcome. We report a case of a 78-year-old diabetic male who was admitted complaining of general fatigue, dark red urine, and vomiting. His blood revealed massive hemolysis. Computer tomography demonstrated huge liver abscess in the right lobe of the liver. About 1 h after admission, he suddenly fell into a critical condition. He died 3 h after admission in spite of intensive care and resuscitation.** ***Clostridium perfringens*** **was detected from the blood taken before death and from liver abscess by biopsy after death. We concluded that this patient died of acute massive intravascular hemolysis in septicemia caused by** ***Clostridium perfringens*** **infection.**

**Key words:** *Clostridium perfringens*, intravascular hemolysis, liver abscess

Massive intravascular hemolysis is a life-threatening complication of *Clostridium perfringens* infection. Prompt recognition of this entity and early therapy offers the only possibility of preventing an otherwise fatal outcome. We present a case of a patient with massive intravascular hemolysis as a result of *Clostridium perfringens* infection.

## Case Report

A 78-year-old diabetic man was admitted to our hospital because of general fatigue, dark red urine, and vomiting. His past medical history was diabetes from about 60 years old. He took glimepride (9 mg) and acarbose (300 mg) for 2 years. His temperature was 36.8 °C and; his conjunctiva was not icteric and he was slightly anemic. His consciousness was clear, but he could not keep still because of malaise. His abdomen was slightly distended but not tender. Computer tomography demonstrated a huge pneumatic abscess in the right lobe of the liver (Fig. 1). His chest sound was clear, and he had no heart murmur. Hemoglobinuria, but not intact red blood cells (RBCs), was found in a urine sample. His blood revealed massive hemolysis, of which the severity was ascertained upon visual examination of blood samples. The blood smear showed marked spherocytosis and with no obvious evidence of microangiopathy (Fig. 2A). Gram staining of a peripheral blood smear revealed a few Gram-positive rods (Fig. 2B). At that time, in an automated blood count, the patient's RBC was $280 \times 10^4/\mu$l, hemoglobin (Hb)

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10.0 g/dl, hematocrit (Ht) 21.6%, mean cell volume (MCV) 77 fl, mean cell hematocrit (MCH) 35.7 pg, white blood cell (WBC) $186 \times 10^2/\mu l$, platelets (PLT) $8 \times 10^4/\mu l$. Total bilirubin concentration was 1.4 mg/dl, AST 5,886 IU/l, ALT 1,155 IU/l, LDH 51,382 IU/l, CPK 40 IU/l, BUN 26.0 mg/dl, Creatinine 0.7 mg/dl. Glucose was 240 mg/dl, HbA1c 6.5%. Room air/arterial blood gas values revealed a pH of 7.34; $PaCO_2$, 19.7 mmHg; $PaO_2$, 41.9 mmHg; calculated $HCO_3$, 10.6 mmol/l; $Na^+$, 126 mmol/l; $K^+$, 5.5 mmol/l; $Ca^{++}$, 0.5 mmol/l; and $Cl^-$, 92 mmol/l. About 1 h after admission, the patient suddenly developed respiratory distress and required mechanical ventilation. A chest radiograph

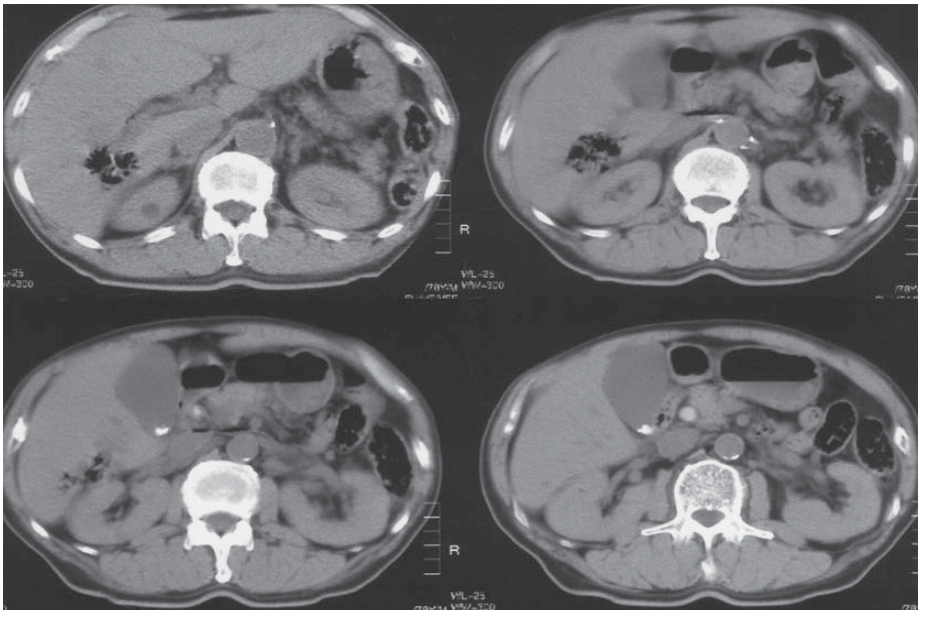

Fig. 1 The abdominal CT scan showed a huge pneumatic abscess in the right lobe of the liver.

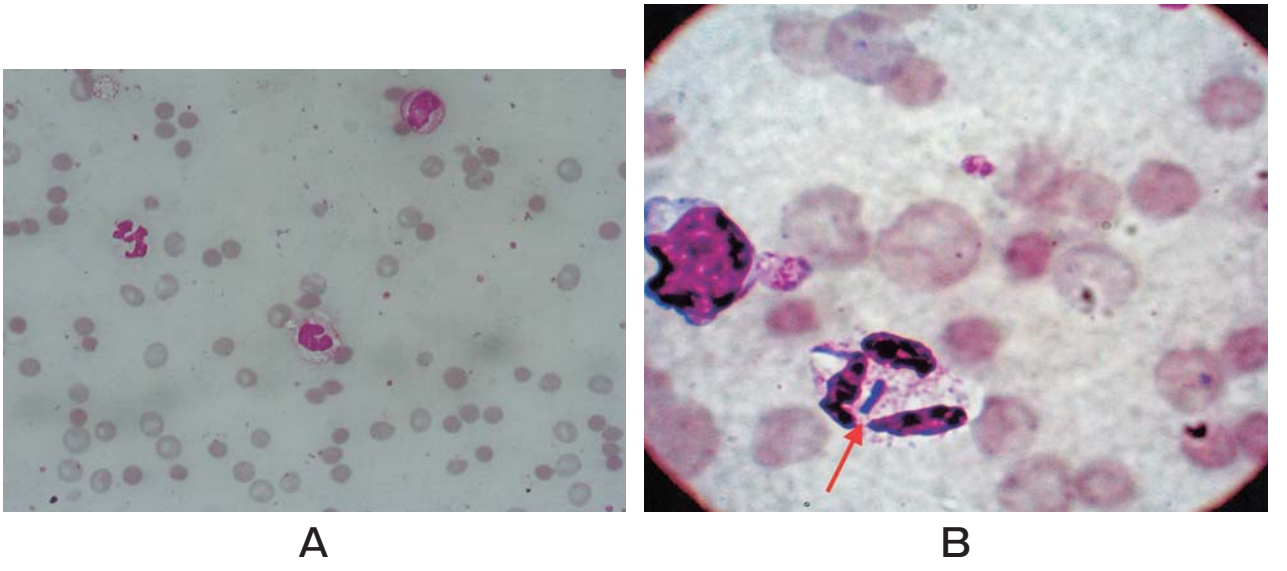


Fig. 2 A, The blood smear showed a lot of irregular erythrocytes in size, but showed no obvious evidence of microangiopathy; B, Gram staining of a peripheral blood smear revealed a few Gram-positive rods.

showed massive lung edema which could not be detected on admission (Fig. 3). Despite aggressive fluid resuscitation, maximal doses of steroid drugs, and mechanical ventilation he subsequently died 3 h after admission. *Clostridium perfringens* was identified in the blood culture taken before death. An autopsy was not performed, but a liver abscess biopsy was performed after death, and *Clostridium perfringens* was also detected from biopsy samples of the liver abscess. We concluded that this patint died of acute massive intravascular hemolysis in septicemia caused by *Clostridium perfringens* infection.

## Discussion

*Clostridium perfringens* is a gram-positive anaerobic bacillus. It is also a commensal bacterium of the human gut [1]. It is encapsulated and produces exotoxins. Gas gangrene occurs when the microorganism attacks soft tissues by producing toxins and aggressins, which are histotoxic [1]. The main toxin is alpha toxin, which is responsible for intravascular hemolysis and the resultant anemia and jaundice [2]. Alpha toxin, one of the many exotoxins produced by *Clostridium*, is an enzyme that splits lecithin into phosphocholine and diglyceride, causing interference with the functional integrity of the red blood cell membrane. This mechanism is postulated to account for the development of spherocytosis and subsequent hemolysis [3].

Individuals especially susceptible to severe clostridial infection include the elderly, diabetic patients, men, patients with hepatobiliary disease and other bowel disease, and patients with other underlying conditions such as leukemia and colon carcinoma [3]. In our case, the patient was elderly, had diabetes with poor control, and suffered from hepatobilirary disease.

There are only a few known infectious and noninfectious diseases that cancause massive intravascular hemolysis. Rarely, infections such as malaria, bartonellosis, babesiosis, and adult hemolytic uremic syndrome (HUS) associated with bacterial infections can cause severe intravascular hemolysis. Other noninfectious causes of severe intravascular hemolysis include incompatible blood transfusions, paroxysmal nocturnal hemoglobinuria (PCH), hemolysis due to lysins such as snake venoms, and extensive acute burns. Our patient's clinical history allowed us to easily exclude malaria, bartonellosis, babesiosis,

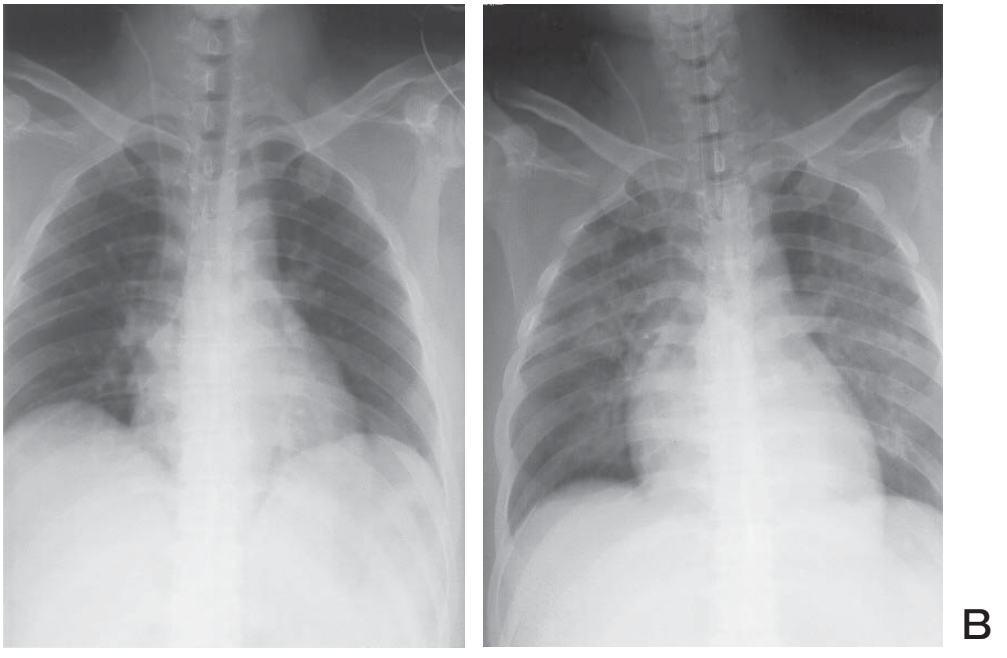


Fig. 3 The chest radiograph on the left was taken on admission (**A**). The chest radiograph on the right, taken 1 h after admission, showed massive lung edema (**B**).

incompatible blood transfusions, PCH, hemolysis due to lysins such assnake venoms, and extensive acute burns. Excluding HUS had to be done by careful diagnosis. HUS is another disorder that can be associated with acute renal failure, thrombocytopenia, and hemolysis. Patients often complain of acute headache with a sudden onset of thrombocytopenia. HUS is occasionally associated with infections such as *Escherichia coli* 0157: H7, *Streptococcus*, and *Shigella*. Unlike *Clostridium perfringens* toxemia, the blood smear will almost always demonstrate microangiopathy [3]. The blood smear of our patient showed marked spherocytosis with no obvious evidence of microangiopathy. This smear result allowed us to exclude HUS.

It is difficult to make a rapid confirmed diagnosis of *Clostridium perfringens* sepsis. Identification of *Clostridium perfringens* in blood culture is usually indispensable for making a confirmed diagnosis. However, when one encounters a drastically affected patint with a massive hemolysis, a blood smear and gram staining will help one to make a rapid diagnosis. In our patient, Gram-positive rods were observed in the blood taken on admission. Gram staining of a peripheral blood smear in a patient with *Clostridium perfringens* sepsis is very useful for giving a rapid diagnosis and identifying causal bacteria [4].

The treatment of choice for *Clostridium perfringens* septicemia is intravenously administered penicillin G in doses of 10 to 24 million units daily and surgical debridement of the infectious focus. In animal and *in vivo* studies, the combination of penicillin and clindamycin has better efficacy than penicillin alone in the suppression of toxin synthesis [3]. Alternatively, *in vitro* studies have also shown chloramphenicol to be effective against all species of *Clostridia*. In one clinical case, immediate antibiotics therapy including penicillin G and metronidazole dramatically stopped hemolysis within a few hours and the patient survived [5]. Surgical debridement of all involved gangrenous tissue is crucial in preventing propagation of the organism and its subsequent exotoxin production [3]. In our patient, the clinical course was so extremely rapid that surgical debridement and penicillin infusion could not be performed, regrettably.

The mortality rate of *Clostridium perfringens* sepsis ranges from 70 to 100 percent [3]. As stated by Dr. Sherwood Gorbach regarding clostridial myonecrosis, "This is a disease that begins where other diseases end with death," [6]. The overall mortality rate is higher when infection induces massive hemolysis [7]. Hemolysis has been considered as the most significant and unfavourable prognostic sign associated with the infection. Alvarez *et al*. reported from a review of 19 patients' cases described in the literature that *Clostridium perfringens*-associated hemolysis emerges as an extremely rapid illness that usually leads to a patient's death within a few hours. They also stated that the few patients who survived were just those in whom treatment had been instituted before the hemolysis became life-threatening [8].

When patients with massive intravascular hemolysis are encountered, hemolysis from *Clostridium perfringens* infection should be considered. Moreover, rapid gram staining of a peripheral blood smear should be performed for differential diagnosis and immediate antibiotics treatment should be started. However, *Clostridium perfringens*-associated hemolysis often leads to a patient's death within a few hours, so the urgent informed consent for treatment and sharing of information about the poor prognosis of this disease are also of great importance for the patient's family and for the medical staff to avoid any suspicion or accusation of about this disease and poor prognosis is also of medical malpractice.

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