CASE REPORT

Clostridium perfringens liver abscess with massive haemolysis

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Liver abscesses are commonly caused by *Enterobacteriaceae* and anaerobes. This report is of a patient with liver abscess with massive haemolysis and multiorgan failure caused by *Clostridium perfringens*. Despite the reportedly high mortality rate and poor prognostic factors, the patient eventually recovered with prompt treatment.

Introduction

Clostridium perfringens septicaemia is a rare, but rapidly fatal, infection. Massive haemolysis is a classical feature of this infection, and may prompt early recognition and treatment. This report is of a patient with *C perfringens* liver abscess with massive intravascular haemolysis and multiorgan failure who was successfully treated.

Case report

A 61-year-old woman was admitted to the Pamela Youde Nethersole Eastern Hospital, Chai Wan, Hong Kong in September 2007, with fever, upper abdominal pain, and vomiting. She had hypertension, diabetes mellitus, and hyperlipidaemia, and had a history of cholecystectomy for unknown reasons.

Blood tests at admission showed leukocytosis and deranged liver and renal functions (Table). Soon after admission to the surgical unit, where she was treated with empirical intravenous cefuroxime (750 mg every 8 hours), ampicillin (1 g every 6 hours), and metronidazole (500 mg every 8 hours) for suspected biliary sepsis, the patient developed respiratory distress due to severe metabolic acidosis (Table). She was transferred to the intensive care unit (ICU), where she was intubated and supported by mechanical ventilation. Continuous venovenous haemofiltration was started for septic shock, multiorgan failure, and severe metabolic acidosis. The ultrafiltrate was noted to be red.

An urgent blood smear revealed the presence of Gram-positive and Gram-negative bacilli. The antibiotics were changed to intravenous meropenem (1 g every 12 hours) and clindamycin (600 mg every 12 hours). Urgent computed tomography of the abdomen and pelvis showed the presence of multiple ill-defined hypo-enhancing lesions with air-fluid levels in the left lobe of the liver. A small amount of pneumoperitoneum was noted in the left subphrenic space. Pneumobilia with a dilated common bile duct (1.6 cm) was present (Fig).

Blood specimens taken from a peripheral vein 10 hours after admission were reported to be unsuitable for analysis due to gross haemolysis on microscopic examination. Repeated blood specimens taken from the radial arterial and femoral venous catheters were in similar conditions and could not be processed. The plasma-free haemoglobin level was markedly elevated to 1361.7 mg/L (reference level, <50 mg/L), consistent with intravascular haemolysis and accounted for the red ultrafiltrate observed. This was supported by subsequent investigations that showed decreased levels of haemoglobin, reticulocytosis, elevated lactate dehydrogenase, and reduced serum haptoglobin to less than 0.06 g/L (Table). A search for the cause of intravascular haemolysis included glucose-6-phosphate dehydrogenase test, blood smear for malaria, Donath-Landsteiner antibody, and direct Coombs' test. All the results were negative. The patient had evidence of disseminated intravascular coagulopathy, but peripheral blood smear did not reveal any schistocytes, suggesting microangiopathic haemolytic anaemia. Blood culture later identified the Gram-positive bacilli as *C perfringens*. *Streptococcus viridans*, *Escherichia coli*, and *Plesiomonas shigelloides* were also identified, and antibiotics were switched to tazobactam-piperacillin (4.5 g every 12 hours) and metronidazole (500 mg every 8 hours) according to the sensitivity pattern.

Emergent exploratory laparotomy was performed 25 hours after admission, which revealed multiple gas-forming liver abscesses, one of which had ruptured into the peritoneal space. Open drainage of the liver abscesses was performed. Endoscopic retrograde cholangiopancreatography was performed 6 days after admission and showed no biliary obstruction.

Key words
Anemia, hemolytic; *Clostridium* infections; *Clostridium perfringens*; Liver abscess; Treatment outcome

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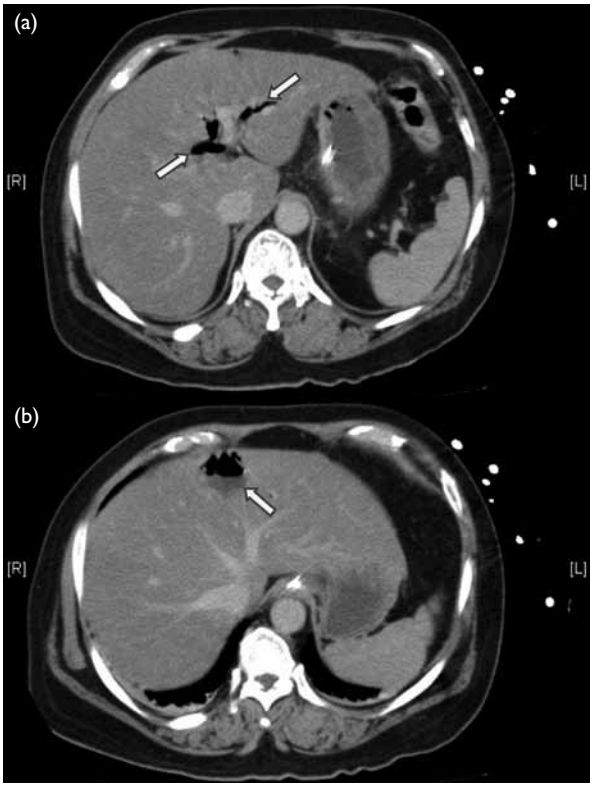

FIG. Computed tomographic images showing (a) pneumobilia (arrows), and (b) gas-forming liver abscess (arrow)

產氣莢膜梭菌肝膿瘍引致的大量溶血

肝膿瘍通常因腸杆菌科及厭氧菌引致。本文報告一名因產氣莢膜梭菌引致肝膿瘍的病人出現大量溶血及多器官功能衰竭。雖然此病過往有高死亡率及較差的預後，因得到及時醫治，這名病人最終得以康復。

The patient gradually improved after abscess drainage and treatment with antibiotics. Further blood specimens showed resolution of haemolysis. She recovered well and was discharged from the ICU 19 days after admission. Her renal function continued to improve and she stopped renal replacement therapy 2 months after admission.

Discussion

Liver abscesses in Hong Kong are usually caused by *Klebsiella* species, *E coli*, and anaerobes.[1] *Klebsiella* was reported to be the most common cause of gas-forming liver abscesses in Taiwan,[2] but massive intravascular haemolysis is not a typical feature. The identification of Gram-positive bacilli septicaemia in the presence of gas-forming liver abscesses with gross haemolysis led to the suspicion of *C perfringens*

TABLE. Serial laboratory results for a patient with liver abscess with massive haemolysis and multiorgan failure caused by *Clostridium perfringens*[*]

Parameter	Baseline	Admission			Results prior to ICU discharge on day 19	Reference range
		Day 1	Day 2	Day 3		
White blood count (x 10^9/L)	5.6	16.8	25.6	12.2	5.0	3.8 to 10.0
Platelets (x 10^9/L)	227	216	259	158	203	150 to 400
Haemoglobin (g/L)	135	143	133	71	71	115 to 160
Sodium (mmol/L)	143	136	Haemolysed	147	137	135 to 146
Potassium (mmol/L)	3.9	4.0	Haemolysed	3.4	3.1	3.5 to 5.0
Urea (mmol/L)	6.3	9.9	Haemolysed	18.5	6.4	2.5 to 6.5
Creatinine (mmol/L)	93	109	Haemolysed	218	440	53 to 97
International normalised ratio	<1.0	1.1	1.4	1.3	<1.0 (day 17)	-
Activated partial thromboplastin time (seconds)	28.2	27.1	74.8	55.5	34 (day 17)	24 to 38
Total protein (g/L)	79	80	Haemolysed	58	55	66 to 87
Albumin (g/L)	46	43	Haemolysed	30	24	35 to 50
Bilirubin (mmol/L)	13	263	Haemolysed	449	10	3 to 17
Alkaline phosphatase (IU/L)	54	112	Haemolysed	139	63	53 to 141
Alanine aminotransferase (IU/L)	20	1314	Haemolysed	587	<6	<41
Amylase (IU/L)	ND	116	ND	ND	ND	25 to 85
Lactate dehydrogenase (IU/L)	ND	ND	ND	4054	717 (day 17)	91 to 180
Haptoglobin (g/L)	ND	ND	Haemolysed	<0.06 (day 7)	2.58	0.16 to 2.00
pH, arterial blood gas	ND	7.098	7.304	7.332	7.484	7.35 to 7.45
Partial pressure of carbon dioxide (kPa)	ND	5.04	5.20	7.99	3.52	4.7 to 6.0
Partial pressure of oxygen (kPa)	ND	35.04	25.61	12.44	14.93	9.3 to 13.3
Bicarbonate (mmol/L)	ND	11.4	18.9	31.0	19.4	21 to 28
Base excess (mmol/L)	ND	-17.5	-6.8	3.4	-2.3	-3 to 3

* ICU denotes Intensive Care Unit, and ND not done

infection. *Clostridium perfringens* is a Gram-positive anaerobic saprophytic bacterium, which can be found in the human gastro-intestinal tract, soil, and sewage. *Clostridium perfringens* grows fast, with a doubling time of only 7 minutes.[3] Like other clostridia, *C perfringens* is capable of producing potent extracellular toxins and heat-resistant spores. These toxins and spores contribute to the spectrum of diseases caused by *C perfringens*, which includes gas gangrene and necrotising enterocolitis of infants. According to the toxin produced, *C perfringens* can be classified into five types. Type A is the most important cause of human diseases.[4]

Clostridium perfringens produces phospholipase C lecithinase (alpha toxin), which has been shown to cause phospholipid hydrolysis in red blood cell membranes, leading to spherocytosis and haemolysis, while production of streptolysin O and perfringolysin O have been implicated in disseminated intravascular coagulation.[4] Testing for the Thomsen-Friedenreich cryptantigen (TCA) might help in earlier diagnosis of clostridial bacteraemia. The presence of TCA on membranes of erythrocytes of patients infected with *C perfringens* has been reported and was postulated to be due to enzymatic cleavage of N-acetyl-neuraminic acid by neuraminidase synthesised by *C perfringens*.[5] N-acetyl-neuraminic acid usually covers the TCA on erythrocytes and its absence may contribute to life-threatening intravascular haemolysis.[5] However, TCA is not a standard test and may not be available in many clinical centres.

Clostridium perfringens septicaemia is associated with a high mortality rate ranging from 70 to 100%.[6] Unlike two fatal cases with similar presentations reported in Japan[7] and Hong Kong,[8] this patient survived despite having a number of poor prognostic factors for liver abscess–related mortality, including ruptured abscess at presentation, hyperbilirubinaemia, prolonged clotting time, and need for emergency laparotomy.[9] Similar to this patient, the patients from Japan[7] and Hong Kong[8] had diabetes. However, the Japanese patient was older at 89 years and he died 3 hours after admission. The patient from Hong Kong was 65 years old and had chronic renal failure and ischaemic heart disease. He died after 3 days despite treatment with broad-spectrum antibiotics, haemodialysis, and peritoneal dialysis. Neither patient underwent drainage of the liver abscess and the antibiotics given to these patients were not stated in the reports. In addition to being younger and having fewer co-morbidities, this patient received appropriate antibiotics early in the course of her illness, as for previously reported patients who recovered.[5,10] She was treated with penicillin, cephalosporin, and metronidazole since the first day of admission to hospital, which were later changed to meropenem and clindamycin, and eventually to tazobactam-piperacillin and metronidazole according to the sensitivity profile. Although in in-vitro studies, *C perfringens* has been shown to be susceptible to almost all penicillins and cephalosporins,[11] these agents are unable to suppress alpha-toxin activity early, and patients remain at risk for fatal toxaemia. By contrast, clindamycin, metronidazole, and rifampin have been shown to rapidly reduce alpha-toxin activity.[12] Experience obtained from the treatment of gas gangrene has shown that a combination of penicillin and clindamycin is the most effective treatment. We are uncertain whether this combination of antibiotics might have offered this patient a survival advantage.

This report illustrates the importance of early initiation of appropriate antibiotics, possibly in combination with abscess drainage, for managing *C perfringens* liver abscesses. Close liaison of ICU physicians, surgeons, microbiologists, and radiologists was crucial for the survival of this patient.

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