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CASE REPORT

A middle-aged lady with a pyogenic liver abscess caused by *Clostridium perfringens*

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Abstract

The pyogenic liver abscess caused by *Clostridium perfringens* (*C. perfringens*) is a rare, but rapidly fatal infection. It is usually associated with malignancy and immunosuppression. We report the case of 50-year-old lady with the secondary liver metastases from rectal cancer presented with fever and epigastric pain. The identification of *Gram-positive bacilli* septicaemia, the presence of gas-forming liver abscess and massive intravascular hemolysis should lead to the suspicion of *C. perfringens* infection. Here we review twenty cases published since 1990 and their clinical features are discussed. The importance of "an aggressive treatment policy" with multidisciplinary team approach is emphasized.

Key words: Pyogenic liver abscess; *Clostridium perfringens*; Infected hepatic metastases; Liver abscess; Gram-positive bacilli septicaemia

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INTRODUCTION

Pyogenic liver abscess caused by *Clostridium perfringens* (*C. perfringens*) is a rare, but rapidly fatal, infection. Massive haemolysis and gas-forming liver abscess are classical features of this infection, which may prompt early recognition and treatment. This report is of a patient with the secondary liver metastases from rectal cancer with *C. perfringens* liver abscess. We also review all the previously reported cases of *C. perfringens* associated liver abscess published in the English literature since 1990 and highlights that this condition is usually associated with malignancy and immunosuppression and should be treated "aggressively" with multidisciplinary team approach.

CASE REPORT

A 50-year-old lady was admitted with epigastric pain and fever in July 2005. She had rectal cancer with multiple liver secondary diagnosed in August 2004 and was managed conservatively. Concerning her present illness, she had acute epigastric pain poorly localized without associated gastrointestinal symptoms. Her temperature was 38.4 ℃, blood pressure 95/64 with pulse 126 bpm. The abdominal examination showed hepatomegly with liver span of 13 cm. Laboratory data were as follow: hemoglobin, 8.3 g/dL (normal, 11.6-15.5 g/dL); white blood cell count, 46.3/mm^3 (normal, 3.9-10.7/mm^3); platelet count, 481/mm^3 (normal, 152-358/mm^3), APTT 38.9 (normal, 24.5-37.6), reticulocyte count, 7% (normal, < 2%); sodium, 136 mmol/L (normal, 136-145 mmol/L); potassium, 3.5 mmol/L (normal, 3.5-5.1 mmol/L); urea,

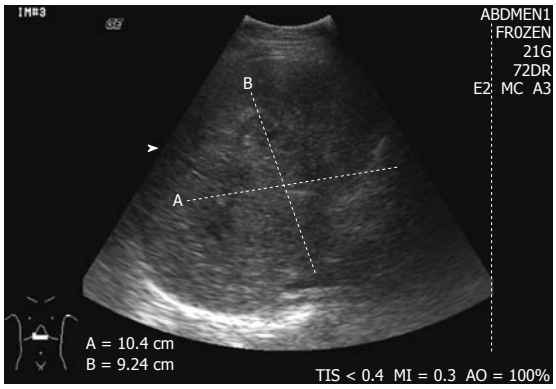

Figure 1 Ultrasound of liver showed mixed heterogeneous echogenicity lesions. Ill defined internal hyperechogenicity with "dirty shadow" appearance suspicious of gas content.

21.2 mmol/L (normal, 2.7-6.8 mmol/L); creatinine, 281 μmol/L (44-80 μmol/L); albumin, 14 g/L (normal, 35-50 g/L); globulin, 43 g/L (normal, no reference); total bilirubin, 153 μmol/L (normal, 5-20 μmol/L); alkaline phosphatase, 302 IU/L (normal, 43-141 IU/L); lactate dehydrogenase 1132 IU/L (normal, 211-370 IU/L). An urgent blood smear revealed the presence of *Gram-positive bacilli* and later identified as *C. perfringens*. She was treated with board-spectrum antibiotic (sulperazone 1 g Q12H and metronidazole 500 mg Q8H intravenously), vigorous fluid resuscitation with inotropic support (dopamine infusion of rate 20 mg/h intravenously) and blood cell transfusion. An urgent ultrasound of the abdomen showed extensive multiple echogenic foci with casting shadows were seen over the right lobe which was compatible with gas-containing space-occupancy lesion (Figure 1). The common bile duct and the gallbladder were normal without any filling defects. The computed tomography of the abdomen and pelvis showed bilobed liver abscesses located at right lobe and segment two/three in which the former (15 cm × 12 cm) had central cavitation and the latter (7 cm × 5 cm) had capsular rupture, resulting in loculated fluid and gas collection medial to the stomach (Figure 2). In addition, the left intrahepatic duct was dilated due to the compression of left lobe abscess. The right-lobe liver abscess was drained percutaneously by ultrasound guided and the left intrahepatic duct obstruction was relieved by transhepatic biliary drainage inserted percutaneously. Nevertheless, her clinical condition deteriorated with multi-organ failure, including acute respiratory distress syndrome and acute renal failure. Finally she was succumbed at seventh day of hospitalization.

DISCUSSION

The patient had typical clinical features of pyogenic liver abscess including fever, epigastric pain, and space-occupancy lesion in imaging and positive blood culture. However, the presence of massive intravascular hemolysis (anemia, reticulocytosis, high lactate dehydrogenase, disproportionate hyperbilirulinemia with relative normal common bile duct), gas-forming liver abscesses and identification of Gram-positive bacilli septicemia should lead to the suspicious of *C. perfringens* infection. The risk factor of our patient was advanced malignancy.

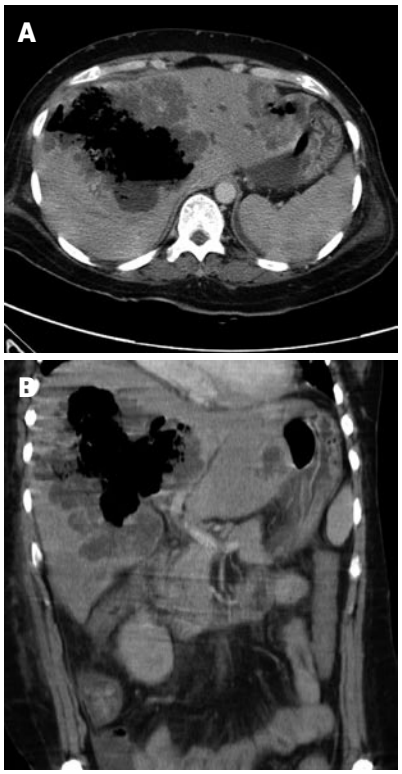

Figure 2 Axial (A) and sagittal (B) contrast multi-detector computerized tomography scan of abdomen. Rim-enhancing cystic lesions with internal gas content occupying both hepatic lobes with the largest occupying the right lobe.

C. perfringens is an ubiquitous, Gram-positive, spore-forming anaerobic bacillus (though, it is not absolute anaerobe as it can tolerate up to 3% O_2). It is normal inhabitant of the human bowel and genital tract. Like other clostridia, *C. perfringens* grows fast with doubling time of about 7 min and its virulence is related to its toxin production which contributes to the pathogenesis of the infection[1,2]. The main toxin is phospholipase C lecthinase (α toxin) which splits lecithin of red cell membrane into phosphocholine and diglyceride and thus damages the structural integrity of the cell membrane. This leads to spherocytosis and subsequent hemolysis. Occasionally, a blood smear can show ghost cells which appear empty because these cells have leaky membrane so that they can no longer retain hemoglobin. α-toxin is also key pathogenic factor in gas gangrene of clostridial soft tissue infection. Other virulence factors act primarily on the vascular endothelium, causing capillary leakage (β-, ε- and τ-toxin). Various risk factors for clostridium septicemia include elderly, poor controlled diabetic mellitus, cirrhosis and malignancy especially gastrointestinal and genitourinary malignancies[3]. In the case presented here, we postulate that the clostridium organisms grew within the devitalized tissue of rectal cancer and then migrated

Table 1 Cases of Clostridium perfringens liver abscesses published since 1990

No.	Author	Year	Age (yr)	Sex	Condition(s)	Hb (g/dL)	Bilirubin (mmol/L)	LDH (U/L)	Focus removed	Survival
1	Batge	1992	61	M	Pancreatic cancer	11.6	752.4	7600	Yes	Yes
2	Rogstad	1993	61	M	None		359.1	1344	No	No
3	Gutierrez	1995	74	M	None	13.1	70	1250	No	No
4	Jones	1996	66	F	Liver transplant	11.3	42.6		No	No
5	Eckel	2000	65	F	Cancer of common bile duct	11.2	78.7	350	Yes	Yes
6	Kreidl	2002	80	M	DM, ESRF		215.5		No	No
7	Pichon	2003	42	F	Alcoholic cirrhosis	10.2	210		No	Yes
8	Quigley	2003	73	M	Ischemic heart	14.2	71		No	No
9	Au	2005	65	M	DM, ESRF	6.2	160.7		No	No
10	Fondran	2005	63	M	Pancreatic cancer				Yes	Yes
11	Daly	2006	80	M	DM	8.7			No	No
12	Ohtani	2006	78	M	DM	10	23.9	51 382	No	No
13	Loran	2006	69	F	None	8.7	170		No	No
14	Agua	2009	74	M	Stroke		32.5		Yes	Yes
15	Merino	2009	83	F	None	12.2	335.2	2288	No	No
16	Meyns	2009	64	M	DM, myelodysplastic syndrome	7.2	141.4	980	No	No
17	Bradly	2010	52	M	Liver transplant		297.5		No	No
18	Ng	2010	61	F	DM	13.5	263	4054	Yes	Yes
19	Rajendran	2010	58	M	None	13.3			Yes	Yes
20	Law	2012	50	F	Rectal cancer	8.3	153	1529	No	No

M: Male; F: Female; ESRF: End stage renal failure; DM: Diabetic mellitus; Hb: Hemoglobin; LDH: Lactate dehydrogenese.

to liver *via* the portal venous system and then began to form local infection in liver parenchyma.

The clinical course of *C. perfringens* septicemia is usually rapidly deteriorated with high mortality rate ranging from 70% to 100%[4]. The treatment of choice is intravenously administrated high-dose penicillin (10-24 million units daily) and surgical debridement of all involved gangrenous tissue, which is thought to be crucial in preventing production of toxins[1]. *In vivo* studies, the combination of penicillin and clindamycin has better efficacy than penicillin alone in the suppression of toxin synthesis. When surgical debridement is difficult, hyperbaric oxygen therapy is worth considering as it can decrease toxin production rate and make the environment less anaerobic for the bacteria to grow because clostridia lack superoxide dismutase, making them incapable of surviving in the oxygen-rich environment created within a hyperoxic tissue[5,6]. The suggested regimen of hyperbaric oxygen is 2-3 atm oxygen for 60-120 min per session with 2-3 sessions per day for up to 6 d. In our case, imaging-guided liver abscess and biliary tract drainage was performed immediately once the diagnosis was made but the primary focus of infection still remained in the rectum. Thus the patient had dreadful outcome.

Since 1990, there are twenty cases of *C. perfringens* liver abscesses published in the English literature (including the current case) (Table 1)[7]. These cases had a median age of 65 years (range 42 to 83 years) and 13 (65%) were male. Five (25%) had the good past health[6,8-11]; four (20%) advanced malignancies, including two pancreatic[12,13], one hepatocellular[14] and one rectal cancer; six (30%) had diabetic mellitus[1,4,15-18], including two complicated with end-stage renal failure, one accompanied with myelodysplastic syndrome and the remaining three having diabetes as the only underlying disorder; three (15%) had cirrhosis[19-21], including two of them treated by liver transplantation and put on immunosuppressive therapy; one had stroke[22] and one had ischemic heart disease[23]. All cases except one (95%) presented with fever and twelve (60%) patients had abdominal pain and eight (40%) did not have localizing signs. One patient suddenly deteriorated and died at home before admission. By using χ^2 test, the abdominal pain was strongly associated with the rupture of the abscess ($\chi^2 = 7.18$, $P < 0.01$). All patients had features of massive intravascular hemolysis on admission, including hemoglobinemia, hemoglobinuria, and microspherocytes in the blood film, highly elevated bilirubin and lactate dehydrogenase. Except the case that died before admission, all cases had early identification of *C. perfringens* in the blood culture. For the morphology of the liver abscess, four (20%) cases were multiple diffuse microabscess; 14 (70%) cases were uniloculated (10 cases located at right and four cases at left lobe); one case was multiloculated at left lobe and one case was bilobed multiloculated. The mean hemoglobin and bilirubin level at presentation were 10.84 g/dL (SD = 2.4 g/dL) and 197.2 mmol/L (SD = 172.1 mmol/L) respectively. The measured hemoglobin level might be falsely high as it measured red cell bound and plasma free hemoglobin. The diagnosis of the liver abscess was made by follow: five cases at autopsy, 13 cases by computed tomography scan imaging and two cases by laparotomy. The indication of laparotomy for diagnosis was the acute abdomen. Only six cases survived (mortality rate of 30%) and five of them had the primary focus of infection removed. By using χ^2 test, their survivals were strongly associated with complete removal of infection focus ($\chi^2 = 11.61$, $P < 0.005$).The median hour of admission death was 11 h. Our patient died on the 7th day that was the longest one among the deaths. We believe this was the result of the

removal of the infected hepatic focus with the primary rectal focus staying behind.

In summary, *C. perfringens* septicemia is a rare but life-threatening disease which requires timely recognition to start an early and specific therapy to prevent mortality.

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