



## Posthepatectomy Liver Failure is More Complex than We Thought

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### Abstract

**Introduction:** PHLF is the most serious complication after hepatectomy. And the reason for PHLF was complex. We report two cases of PHLF accompanied with elevated PCT and low-density area examined by CT.

**Case Presentation:** A 44 year old male experienced left lobe hepatectomy due to carcinoma rupture and a 48 year old male underwent hepatic pancreas to duodenectomy because of duodenal neuroendocrine tumor with liver metastasis. Both patients had elevated INR and bilirubin on POD 5 and POD12, respectively. We eliminated the common reason for PHLF and excluded the reason of PCT elevation besides infection. Therefore, infection was deemed to be the reason caused PHLF in our cases. Then, antibiotics were given, the patient recovered gradually both in liver function and CT image. This observation highlights the complexity of the disease and the value of PCT and CT in the patient who underwent Posthepatectomy.

**Conclusion:** We recommended PCT as a routine monitoring marker in the patient undergoing hepatic resection. And CT was mandatory when PCT elevated coupled with liver function deterioration.

**Keywords:** Posthepatectomy liver failure; Procalcitonin; Computed tomography

### Introduction

Breakthrough in technology and improved postoperative management make it possible to perform hepatic resection more successfully. However, postoperative complications limited its extensive application, especially the Post Hepatectomy Liver Failure (PHLF). PHLF is the major cause of mortality after hepatic resection. The reasons for PHLF are complex, and include small future liver remnant, infection, liver ischemia, prolonged vascular occlusion, ligated outflow but missed inflow vessel and prolonged rotation [1]. Here, we report two cases of PHLF caused by infection and successfully managed by noninvasive treatment.

### Case Presentation

#### Case 1

A 44-year-old man was referred to our hospital due to abdominal pain. An urgent CT scan showed a tumor located in the left lobe of the liver accompanied by tumor hepatic rupture. He had no history of weight loss or jaundice. He denied a history of smoking and alcohol abuse. The baseline characteristics of the patient are presented in Table 1. There was no positive sign on physical examination. However, un-coagulated blood was observed by diagnostic abdominal paracentesis. After admission, the blood pressure and hemoglobin decreased gradually. Transcatheter Arterial Embolization (TAE) was performed to control bleeding. However, the hemoglobin decreased again. Then left hepatectomy was performed. The patient's blood pressure and hemoglobin were stable and his liver function recovered at first. But the patient's liver function deteriorated suddenly and urgent CT showed a large low-density area with no enhancement on contrast-enhanced CT scan in the remnant liver on Post-Operative Day (POD) 3. The elevated Pro Calcitonin (PCT) level

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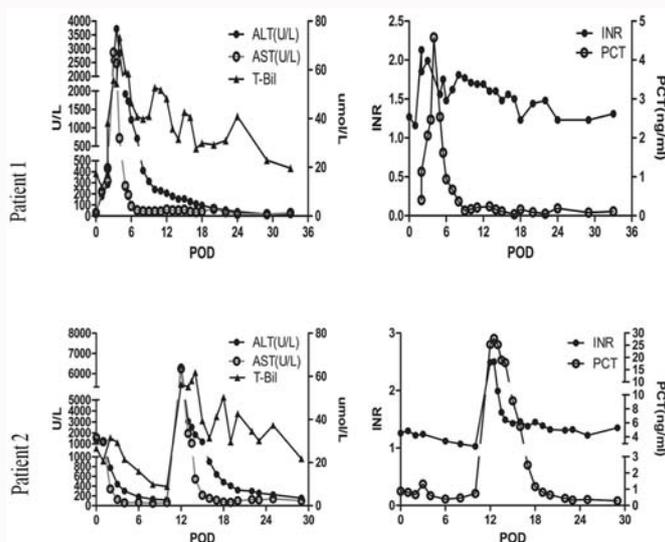


Figure 1A: Dynamic changes of liver function and PCT level in the patients.

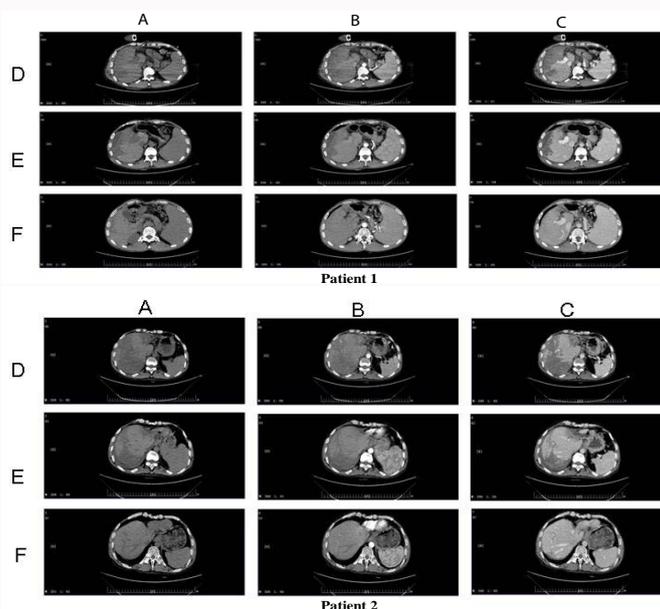


Figure 1B: Abdominal CT scan shows a low-density area in the liver. A: hepatic equilibrium phase; B: hepatic arterial phase; C: portal venous phase. D: time of liver function deteriorated; E: 15 days after PHLF. F: 6 months after PHLF.

was suggestive of infection. Antibiotics, plasma and liver protecting medicine were then administered, the PCT level decreased and the patient recovered gradually both in liver function (Figure 1A, Patient 1) and CT findings (Figure 1B, Patient 1). During a 15-month postoperative follow-up, no sign of local recurrence or distant metastasis was observed.

**Case 2**

A 48-year-old man was admitted to our hospital with liver tumors of unknown origin. He had no history of weight loss, abdominal pain or jaundice. He denied a history of smoking and alcohol abuse. No family or genetic history was found. There was no positive sign on physical examination. Electrocardiogram and chest radiography were normal. The baseline characteristics of the patient are presented in Table 1. Abdominal CT scan and SPIO-enhanced MRI showed two lesions located in the liver. Secondary liver cancer was initially suspected.

However, no tumors were found by esophagogastroduodenoscopy and colonoscopy. Since malignant liver lesions were suspected, a multi-disciplinary consultation suggested biopsy and PET-CT for further investigation of these lesions, and better assessment of the extent of disease. However, the patient chose to surgery directly. After appropriate preoperative preparation, the patient underwent exploratory laparotomy. This exploration showed a new lesion of 1 cm × 1 cm located on the descendant duodenum near the head of pancreas and two lesions located on the left lobe and segment VI of the liver. Hepatic pancreateo duodenectomy was performed as no other lesions were found. The patient recovered well until POD 12. On POD 12, the patient’s liver function deteriorated suddenly, PCT increased and CT scan showed the same change of the remnant liver as in patient 1. PHLF was diagnosed. The same treatment was given as for patient 1. The patient recovered gradually both in liver function

(Figure 1A, Patient 2) and CT findings (Figure 1B, Patient 2). During a 12-month postoperative follow-up, no sign of local recurrence or distant metastasis was observed.

## Discussion

International Study Group of Liver Surgery (ISGLS) proposed the following diagnosis criteria for PHLF in 2010 [2]: elevated International Normalized Ratio (INR) (or clotting factors are needed to maintain normal INR) and hyperbilirubinemia (according to the normal cut-off levels defined by the local laboratory) on or after POD 5. In the present cases, both patients had elevated INR and bilirubin on POD 5 and POD12, respectively. A diagnosis of PHLF was established. The reason for PHLF is complex. And small-for-size syndrome was deemed to be the most common cause [3]. We calculated the remnant liver volume and performed Indocyanine Green Test (ICG) before operation. Both patients had more than 50% future liver remnant and normal ICG, and low risk for PHLF. The low-density area in the remnant liver shown on CT indicated that the liver may have abnormal blood supply. However, the hepatic artery and portal vein branch were clear found and most ischemic injure in liver located in sub capsular and wedge shaped. That CT scanning excluded both vascular embolism and biliary obstruction. This is confusing, as elevated PCT-associated infection may result in PHLF. Nevertheless, the relationship between infection and PHLF is complex. Infection may lead to liver failure while liver failure may cause susceptibility to infection. In our cases, PCT elevation is synchronous with liver function deterioration. And the decrease of PCT was coincided with the recovery of liver function. These indicated that infection is the cause of PHLF in our cases.

PCT, the prototype of a hormokine mediator, is released from all cell types throughout the body by microbial infections and is regarded as a reliable marker of sepsis [4]. Serum PCT levels may elevate in the presence of neoplasm, especially in medullar carcinoma of the thyroid and small-cell lung carcinoma [5], nevertheless both our patients had normal PCT level before liver function deterioration. These demonstrated that PCT elevation was not associated with tumor in our patients. The value of PCT to identify bacterial infection in liver failure patients is controversial [6,7]. PCT elevation appears to be associated with hepatic necrosis in Acute Liver Failure (ALF) [6]. Mallet reported that PCT was an accurate predictor of bacterial infection in patients with ALF unrelated to acetaminophen intoxication [8]. In the present cases, the patients had no history of acetaminophen administration. Although body temperature was normal, the high PCT level indicated bacterial infection. After antibiotics treatment, PCT decreased and the patients recovered both in liver function and CT findings. These indicated that PCT is a reliable marker in PHLF caused by infection.

The CT scanning change was interesting in our patients. Initially, vascular embolism and biliary obstruction disease were excluded and there was a large low-density area in the remnant liver. The low-density area was reduced and liver function recovered and restored to normal subsequently. The dynamic change indicated that the liver experienced denaturation rather than necrosis. Furthermore, this change also excluded the elevated PCT caused by liver necrosis. These results showed that CT is important for the diagnosis of PHLF caused by infection.

Some unique characteristics should be noted in these cases as well. First, PCT is a valuable indicator in PHLF patients. Second,

**Table 1:** Baseline characteristics of the two patients.

Characteristic	Patient 1	Patient 2
Age(yr)	44	48
Gender	Male	Male
History of HBV infection	Yes	No
Tumor location in liver segments	II,III,IV	II,III,IV,VI
Tumor makers		
AFP (0-8.1)	1.3	1.3
CEA (0-5)	0.5	1.29
CA19-9 (0-30.9)	14.52	15.8
ICG R15	5	1.3
C-P	A6	A5
FLR	60%	53%
Duration of operation (min)	260	540
Vascular occlusion time (min)	10,17	10,10,10,10
Blood loss (mL)	500	1200
Blood transfusion (mL)	1200	800
Blood culture	Negative	Negative
Drainage culture	Negative	Negative
Drainage smear	Negative	Negative
pathological diagnosis	HCC	Neuroendocrine tumor (G2)

HBV: Hepatitis B Virus; AFP:  $\alpha$ -fetoprotein, CEA: Carcinoembryonic Antigen; CA19-9: Carbohydrate Antigen 19-9; ICG: Indocyanine Green Test; C-P: Child-Turcotte-Pugh Classification; FLR: Future Liver Remnant

CT scanning changes are observed when the patients develop PHLF caused by infection. Third, the second patient developed PHLF on POD 12, indicating that PHLF may occur at any time.

The limitations in this study included a small number of cases, and absence of liver biopsy, and the CT scanning changes need further study.

In conclusion, our data indicate that infection is important for the development of PHLF. This observation highlights the complexity of the disease. We recommend PCT as a routine monitoring marker in the patient undergoing hepatic resection. And CT scan is mandatory when PCT elevates with deteriorated liver function in these patients.

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