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A case of necrotizing pancreatitis subsequent to transcatheter arterial chemoembolization in a patient with hepatocellular carcinoma

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Necrotizing pancreatitis is one of the rare complications of transcatheter arterial chemoembolization (TACE). Necrotizing pancreatitis after TACE may result from the development of ischemia caused by regurgitation of embolic materials into the vessels supplying the pancreas. We report a case of post-TACE necrotizing pancreatitis with abscess formation in a patient with hepatocellular carcinoma. The patient had suffered hepatic artery injury due to repetitive TACE; during his 25th TACE procedure he had submitted to selective catheterization of the feeding vessel from the dorsal pancreatic artery with a cytotoxic agent and Gelfoam particles. The patient complained of abdominal pain after the TACE procedure, and a CT scan led to a diagnosis of necrotizing pancreatitis with abscess formation. The pancreatic abscess progressed despite general management of the pancreatitis, including antibiotics. Percutaneous catheter drainage was performed, and the symptoms of the patient improved. **(Clin Mol Hepatol 2012;18:321-325)**

Keywords: Carcinoma, Hepatocellular; Therapeutic chemoembolization; Acute necrotizing pancreatitis

INTRODUCTION

Hepatocellular carcinoma (HCC) is the fifth most common malignancy in the world and its incidence is increasing.[1] But, HCC is usually found in advanced stages and often associated with other comorbidities, making curative therapies only be applicable to less than 30-40% of the patients.[2]

In HCC patients who cannot be candidates for curative therapies transcatheter arterial chemoembolization (TACE) is currently the mainstay of palliative treatment. Multiple trials show that TACE increases objective tumor responses, slows tumor progression and improves survival benefits.[3,4] However, TACE can lead to several possible complications, although lethal result is very uncommon. Common complications include post embolization syndrome, fever, intrahepatic biloma, cholecystitis, splenic infarction, gastrointestinal mucosal lesions, multiple intrahepatic aneurysms, and rare but more severe complications include acute hepatic failure, pulmonary embolism or infarction, tumor rupture, hepatorenal syndrome, and variceal bleeding.[5] Although the incidence of acute pancreatitis after TACE has been reported to be various between 1.7-40%, a few case of necrotizing pancreatitis complicating abscess formation after TACE have been reported.[6,7] The risk factors associated with acute pancreatitis after TACE were un-selected angiography, numbers of procedures, and the volume of embolic material. We describe a necrotizing pancreatitis with abscess following TACE in a patient with HCC.

Abbreviations:

HC, hepatocelluar carcinoma; TACE, transcatheter arterial chemoembolization; CT, computed tomography; PCD, percutaneous catheter drainage; MPD, main pancreatic duct

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CASE REPORT

A 69-year-old man with HCC complicating hepatitis B virus-related cirrhosis (Child-Pugh class A) was admitted for 25th TACE. On admission, the patient had no clinical symptoms, and clinical examination was normal except mild hepatomegaly. Laboratory findings were as follows: hemoglobin 11.3 g/dL, white blood cell count 4,000/μL, platelet count 144,000/μL, Albumin 3.0 g/dL, AST 38 IU/L, ALT 20 IU/L, alkaline phosphatase 150 IU/L, GGT 127 IU/L, total bilirubin 1.02 mg/dL, prothrombin time 15.9 seconds. Abdominal computed tomography (CT) confirmed the presence of viable HCCs in segment 1, 3 and 7, and occlusion of both hepatic arteries was seen due to repetitive TACE. TACE was performed with selective catheterization of the dorsal pancreatic artery branches feeding the tumors with a mixture of lipiodol (4 mL), cytotoxic agent (adriamycin 15 mg), and gelfoam (Fig. 1 A, B).

After TACE, the patient complained of poor appetite, nausea, and abdominal pain. On the post-procedure day, the patient had fever, and his laboratory results showed mildly increased AST (50 IU/L), ALT (23 IU/L), and total bilirubin 2.03 mg/dL. The patient's symptoms were treated conservatively; hydration, pain and fever control, accordance with post embolization syndrome. On the 5th day, because his fever and abdominal pain were controlled by oral medications and the patient was discharged.

Five days later, the patient was re-admitted for abdominal pain. His vital sign was stable and abdominal examination revealed severe epigastric tenderness with palpable tender mass. The liver enzyme levels were similar as before admission, but the white blood cell count 10,900/μL, C-reactive protein 90.62 mg/L, serum amylase 200 IU/L and lipase 153 IU/L levels were elevated. Abdominal CT images demonstrated swelling of the pancreas and focal areas of low density in the pancreas body, suggesting necrosis. Peripancreatic fluid collection with thick, enhancing wall is noted. Necrotizing pancreatitis with infected pseudocyst was diagnosed (Fig. 2).

The patient was treated for 5 days with general management of acute pancreatitis: pain control, hydration, fasting and total parenteral nutrition. The patient's symptoms improved, and serum amylase and lipase level decreased to 102 IU/L, 49 IU/L, respectively and oral diet was permitted.

Two weeks later, the follow up abdominal CT showed that slightly decreased fluid collection of the peripancreatic space, but a 2.4 cm sized fluid collection in the posterior aspect of stomach was newly developed. Because of pancreatic duct amputation was identified in the abdominal CT scan, this could have caused the evolution of the new lesion. The patient's condition was stable after oral diet, scheduled ERCP was performed with the object of pancreatic duct stenting. The guide-wire was not able to pass into the main pancreatic duct (MPD) of the body portion due to the acute angulation of the MPD of the neck. Since stent insertion through the pancreatic duct failed, two 10 F pigtail-tipped drainage catheters were inserted into the abscess cavities to enable percutaneous catheter drainage (PCD) (Fig. 3). Blood and bile culture were taken and empirical antibiotics (ciprofloxacin 200 mg per 12 hour) were started. *Klebsiella pneumoniae* that was resistant to quinolone and sensitive to 3rd generation cephalosporin, was identified from the culture of the abscess pocket drainage through the PCD catheter and we changed the antibiotics from

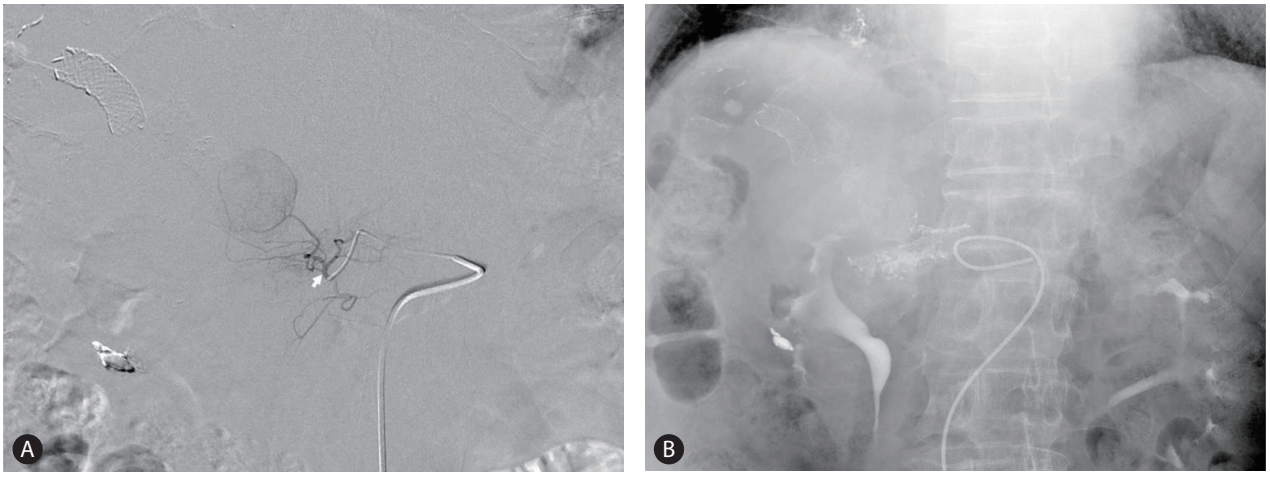

Figure 1. (A) Selective angiography of the parasite tumor-feeding vessel from the dorsal pancreatic artery (arrow) demonstrating the tumor nodule, and regurgitation of the embolic material into the dorsal pancreatic artery (arrowhead). (B) The patient's 25th TACE, which was performed with a mixture of Lipiodol, Adriamycin, and Gelfoam.

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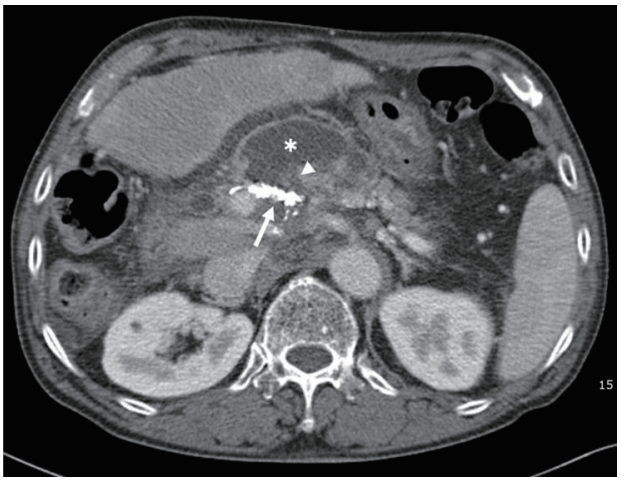

Figure 2. Abdominal CT image showing pancreatic swelling and a low-density area in the pancreas (arrowhead), suggesting necrosis. Dense Lipiodol accumulation in the dorsal pancreatic artery (arrow) and peripancreatic fluid collection (asterisk) with a thick enhanced wall were also noted. Necrotizing pancreatitis with an infected pseudocyst was diagnosed.

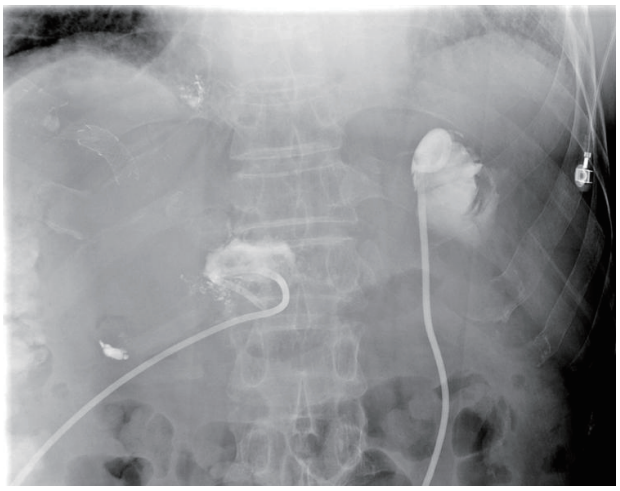

Figure 3. Pigtail-tipped catheters for percutaneous drainage were inserted into the abscess cavities of the patient.

ciprofloxacin to cefotaxime. Two weeks after the antibiotic was changed, extended-spectrum beta-lactamase producing *Klebsiella pneumoniae* and cefotaxime resistant *Citrobacter freundii* were identified in the repeated abscess culture. Since both of the bacteriaes were sensitive to carbapenem, the antibiotic was changed to ertapenem. Abdominal CT scan was performed again on hospital day 30, and fluid collection in the body portion of the pancreas was decreased. The amount of drainage through PCD was decreased and the drainage catheters were removed.

After a week, the superficial cystic lesion was palpable in the drainage catheter removal site of the patient. Abdominal CT showed fluid collection along the previous drainage catheter insertion tract continuous with the previous fluid collection between the stomach and the pancreas. The patient underwent recanalization and percutaneous drainage catheter was reinserted. Methicillin-resistant *Staphylococcus aureus* was identified from the culture of the fluid drainage through the PCD catheter, and vancomycin was added to ertapenem. Two weeks later, the patient's symptoms were improved, the amount of drainage through PCD was decreased, and the serum amylase level was normalized. Finally, on the 71st hospital day, the patient was discharged. The necrotizing pancreatitis with abscess formation was improved but the patient's liver function deteriorated. Patient was still alive, but the further active treatment of HCC could not be possible because of deterioration of liver function.

DISCUSSION

Currently, TACE has been implemented more widely, however, complications of TACE are still an issue. The common complication of TACE, the post embolization syndrome, is benign with abdominal pain (26-55%), vomiting (17-50%) and fever (33-55%). Severe complications occur in 2-7% of the patients.[4,8] Extrahepatic uptake of chemoembolization material in other organs is relatively common but usually does not cause any problems. Complications related to ischemic injury due to embolic material: acute cholecystitis (1-8%), duodenal ulcerated complications (1-10%) and acute pancreatitis are rare. Among them, acute pancreatitis has an incidence ranging from 1.7% (acute clinically overt pancreatitis) to 40% (biological pancreatitis), but fatal outcome is generally low (1-2%).[9]

The risk factors associated with acute pancreatitis after TACE were non-selected embolization, the numbers of procedures, and the volume of embolic material.[9,10] Ischemic damage to the pancreas is usually due to the embolization of the vessels supplying the organ because of the regurgitation of the embolic materials. As the relationship between the catheter tip position and pancreatic tissue damage was clearly established, a lower frequency of acute pancreatitis after TACE was shown by performing superselective TACE in comparison with non-superselective TACE.[11,12] Hepatic artery injury due to repetitive TACE can cause the development of parasitic tumor feeding vessels from the non-hepatic artery, which can increase the extrahepatic ischemic injury. There have been reports that the injecting of more than 2 mL embolic

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material compared to less than 2 mL caused a significant increase in the incidence of acute pancreatitis. From the anatomic variation aspect, when many vessels arise from a common trunk with early bifurcation, this can affect the chance of developing ischemic injury, and the severity of the injury. Moreover, the performer of the procedure needs to exercise caution because, in advanced atherosclerosis patients, the iatrogenic dissection of the gastroduodenal artery during the procedure can cause acute pancreatitis through the ischemic mechanism because since the anastomosis of the superior pancreaticoduodenal artery and the superior mesenteric artery can be ineffective. Thus, precaution regarding the development of acute pancreatitis after TACE is needed in patients who have had repetitive procedures, who have been injected with large amounts of embolic material, and who have had nonselective TACE.

To prevent this complication, it is important to reduce backflow embolic material by placing the catheter tip as close to the distal branches of hepatic artery as possible, and embolic materials should be injected carefully to avoid the regurgitation.[13]

In the case reported herein, repetitive TACE caused total occlusion of the proper hepatic artery injury, As such, a parasitic tumor feeding vessel was developed from the dorsal pancreatic artery. TACE with selective catheterization of the dorsal pancreatic artery branches can increase the pancreas ischemic injury. In this case, the embolic materials were found in the dorsal pancreatic artery in the abdominal CT after TACE. Even if an embolic regurgitation event is not seen, however, it is important to consider the possibility of the development of acute pancreatitis after TACE. It is difficult to differentiate between early onset pancreatitis and post TACE syndrome based on symptoms like abdominal pain and nausea. In the patient in this case report, amylase and lipase levels were not checked early, the delay in the management of acute pancreatitis may have contributed to the worsening of the symptoms. Therefore, in patients who complain of abdominal pain after TACE, it is very important consider the possibility of the development of acute pancreatitis and to measure the serum pancreatic enzymes.

The treatment of pancreatitis induced by chemoembolization for the treatment of HCC is conservative, as in acute pancreatitis from other causes. Prophylactic antibiotics were administered in all the cases where pancreatic necrosis was evident in the CT scan, to avoid bacterial translocation from the gut. In the case reported herein, conservative management was the mainstay of the treatment with external drainage, because infection of the necrotic tissue was suspected. Generally, open surgery is considered the gold standard for infected pancreatic necrosis, but surgical intervention is associated with considerable morbidity. Therefore, a minimally invasive technique, such as PCD has an increasingly important perceived role in the management of pancreatic abscess, and of infected pancreatic necrosis in patients with underlying diseases such as liver cirrhosis.[14]

In conclusion, necrotizing pancreatitis with abscess formation is a rare complication of TACE, and may mimic postembolization syndrome at the early stage. The awareness of this complication, and in patients complaining of abdominal pain after TACE, routine monitoring of the serum pancreatic enzymes, are important in the early detection and treatment of acute post procedural pancreatitis.

Conflicts of Interest

The authors have no conflicts to disclose.

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