

Duodenal perforation and esophageal ischemia following transarterial chemoembolization for hepatocellular carcinoma

A case report

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Abstract

Transarterial chemoembolization (TACE) is frequently used for treatment of unresectable hepatocellular carcinoma (HCC) and can also be used for case of liver metastases from rectal cancer. Although it is recognized as safe and effective treatment, various complications have been reported. However, post-TACE duodenal perforation with duodenal and esophageal ischemia has not been reported in the literature. A 43-year-old male had experienced duodenal perforation combined with duodenal and lower esophageal ischemia after 8 times of repeated TACE for recurrent and unresectable HCCs, that was confirmed on esophagogastroduodenoscopy and abdominal computed tomography. Interestingly, operative findings showed complete recovery of duodenal ischemia except perforation, and he recovered with just the segmental duodenectomy and gastrojejunostomy. We report a case of duodenal perforation with necrosis and esophageal ischemia after 8th TACE for unresectable HCC. Although this complication is rare and unexpected, it may result in severe sequelae requiring surgical repair.

The careful procedure during TACE followed by post-TACE careful monitoring is required in patients with posthepatectomy or repeated TACE, especially in the case with unusual clinical manifestations.

Abbreviations: APCT = abdominal pelvic computed tomography, CT = computed tomography, EGD = esophagogastroduodenoscopy, HCC = hepatocellular carcinoma, PCD = percutaneous drain, TACE = transarterial chemoembolization.

Keywords: duodenal ischemia, duodenal perforation, esophageal ischemia, hepatocellular carcinoma, transarterial chemoembolization

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Advance in Knowledge and Implication for Patients Care: Post-TACE duodenal and esophageal ischemia with duodenal perforation is rare complication and unexpected, it may result in severe sequelae requiring surgical repair. Therefore, careful procedure during TACE followed by post-TACE careful monitoring is required in patients with post-hepatectomy or repeated TACE, especially in the case with unusual clinical manifestations.

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1. Introduction

Transarterial chemoembolization (TACE) is the mainstay for the unresectable intrahepatic hepatocellular carcinoma (HCC).^[1] It can be used for HCC with portal vein tumor thrombosis or single large HCC.^[2,3] In addition, it was reported that TACE can be effective for unresectable liver metastasis in patient with rectal cancer.^[4] Despite the relative safety of TACE, this procedure has many possible complications such as mild fever, abdominal pain, nausea, vomiting, and so on.^[5] These common symptoms have been considered as postembolization syndrome,^[5] and conservative treatment is sufficient for them.

The duodenum and esophagus are supplied with blood from several arteries, and theoretically, ischemia of these organs usually does not develop. In HCC patients with underlying duodenal ulcer, TACE can be stressful event, and it may aggravate duodenal ulcer resulting in duodenal perforation. However, this case showed extensive mucosal injury in duodenum and esophagus rather than focal duodenal mucosal damage. Although a case report about post-TACE acute ischemic duodenal ulcer was reported,^[6] post-TACE duodenal perforation with duodenal and esophageal ischemia has not been reported in the literature.

In this report, we present a case of post-TACE duodenal perforation combined with duodenal and low esophageal ischemia after the 8th repeated TACE for unresectable HCCs.

2. Case report

A 43-year-old male was admitted to our hospital for an 8th session of transarterial chemoembolization (TACE). He had a

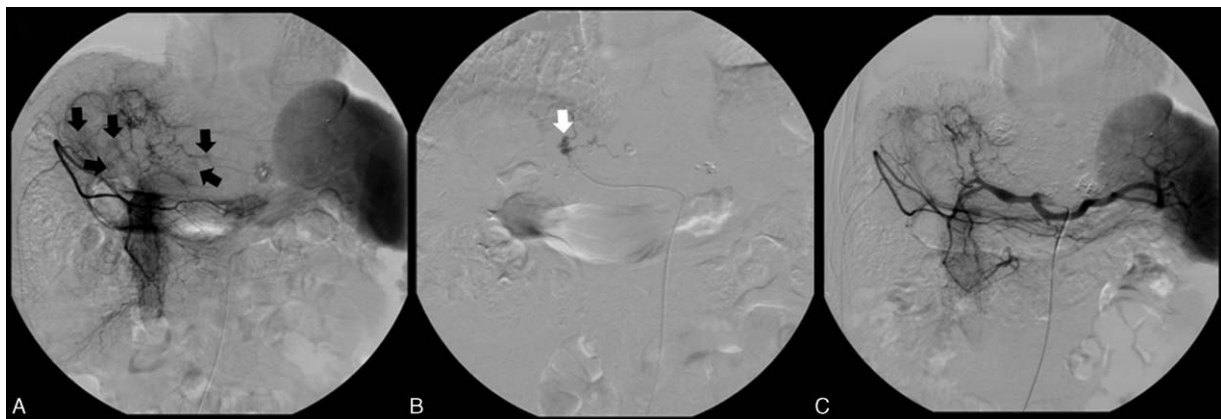


Figure 1. Celiac arteriogram showed ill-defined hypervascular tumor stainings scattered multifocally in remnant left lobe (A, black arrow). Embolization by gelform and lipiodol was performed after superselection of left hepatic artery (B, white arrow). Tumor staining scattered in left lobe disappeared in postembolization celiac arteriogram (C).

20-year history of 60g/day of ethanol consumption and had chronic hepatitis B-related liver cirrhosis at the time of initial diagnosis with HCC. Initially, he underwent right hemihepatectomy for 16-cm-sized single large HCC in right lobe. Six months later, follow-up dynamic liver computed tomography (CT) revealed multiple arterial enhancing and delayed wash-out lesions in remnant liver. Since then, 7 times of repeated TACE had been performed with 1- or 2-month intervals. Laboratory test results at time of admission for the 8th TACE were as follows: alanine transaminase 18IU/L, alpha-fetoprotein 3.4 ng/mL, protein-induced vitamin K absence II 525 mAu/mL, total bilirubin 0.7 mg/dL, albumin 3.6 mg/dL, and prothrombin time INR 1.09. Other laboratory findings including complete blood count concentration were within normal limits.

The patient underwent the 8th TACE (Fig. 1) without any immediate complication except for mild nausea and vague dull pain on right upper quadrant abdomen that were developed right after TACE. Vital signs after 8th TACE were stable as followings; blood pressure 123/83 mm Hg, heart rate 65 bpm, respiratory rate 18/min, and temperature was 36.6°C. On the second day after TACE, severe and sharp pain with tenderness developed on epigastric area, but there was no rebound tenderness or fever. Furthermore, this pain with tenderness improved on the 3rd day after TACE despite persistence of nausea and vague abdominal discomfort. From the 6th day after TACE, laboratory finding showed decreased hemoglobin level (10g/dL), but vital sign maintained stable.

On the 7th day after TACE, esophagogastroduodenoscopy (EGD) was performed to evaluate the cause of anemia, and it showed unexpected duodenal and esophageal ischemia (Fig. 2A and B). Although perforated duodenal wall was not detected during EGD, abdominal pelvic CT (APCT) images revealed pneumoperitoneum and multifocal loculated fluid collection with air fluid level around duodenum and stomach, and in right anterior pararenal space (Fig. 2C). After the review of simple abdomen and chest x-ray, there had been already free-air in the subphrenic area from the 3rd day after TACE (Fig. 3). However, there was no free-air in the intraabdominal x-rays on the first and second day after TACE.

Percutaneous drain (PCD) was emergently inserted into loculated air-fluid region, and a nasogastric tube was emergently placed right after detection of duodenal perforation on APCT. The patient was therapeutically fasted, and intravenous

hydration and intravenous broad spectrum antibiotics were administered. On the 11th day after TACE, follow-up APCT images depicted improvement of the extent of duodenal wall edema and of the some air-fluid pockets around PCDs. However, perforation size of duodenal wall did not decrease (Fig. 2D). Since the patient's hemodynamic status was consistently stable, elective surgical treatment was performed on the 15th day after TACE. Interestingly, operative findings showed complete recovery of duodenal ischemia except perforation (Fig. 4A). The patient underwent just the segmental duodenectomy and gastrojejunostomy alone rather than Whipple operation or pylorus preserving pancreaticoduodenectomy (Figs. 4A and B). Postoperative histological specimen showed ruptured edge of duodenal wall shows abrupt discontinuity of muscle layer with granulation tissue formation, mucosal necrosis and subserosal inflammation, and hemorrhage (Fig. 5). After discharge without any complication, the patient has visited outpatient clinic for regular monitoring of HCC. The study was approved by the Institutional Review Board of Inha University Hospital, Incheon, South Korea.

3. Discussion

TACE is known to be safe as well as effective for HCC, but the vascular and nonvascular complications have been reported.^[5,7,8] Among the nonvascular complications, postembolization syndrome occurs up to 90% of patients following TACE,^[5] and it is usually self-limited in <48 hours.^[9] Beside the postembolization syndrome, many nonvascular complications are known, such as hepatic abscess and biloma, bacteremia, hepatic failure, renal failure, pancreatitis, and hematologic toxicities induced by chemo-agents.^[5,7,8] However, mucosal necrosis in duodenum and esophagus with duodenal perforation has not been reported. Therefore, this case report is meaningful.

In this case, mild nausea that developed right after TACE was initially regarded as one of the symptoms of postembolization syndrome. However, the sudden onset of severe epigastric pain with abdominal distention could not be considered as simple postembolization syndrome. Moreover, slightly ongoing anemia could be a clue for possibility of gastrointestinal complication despite the absence of hemodynamic instability. Simple chest or abdominal x-ray could also be an important image modality for detection of bowel perforation. However, in this case, abdominal fat and ascites that was caused by pre-TACE hydration prevented

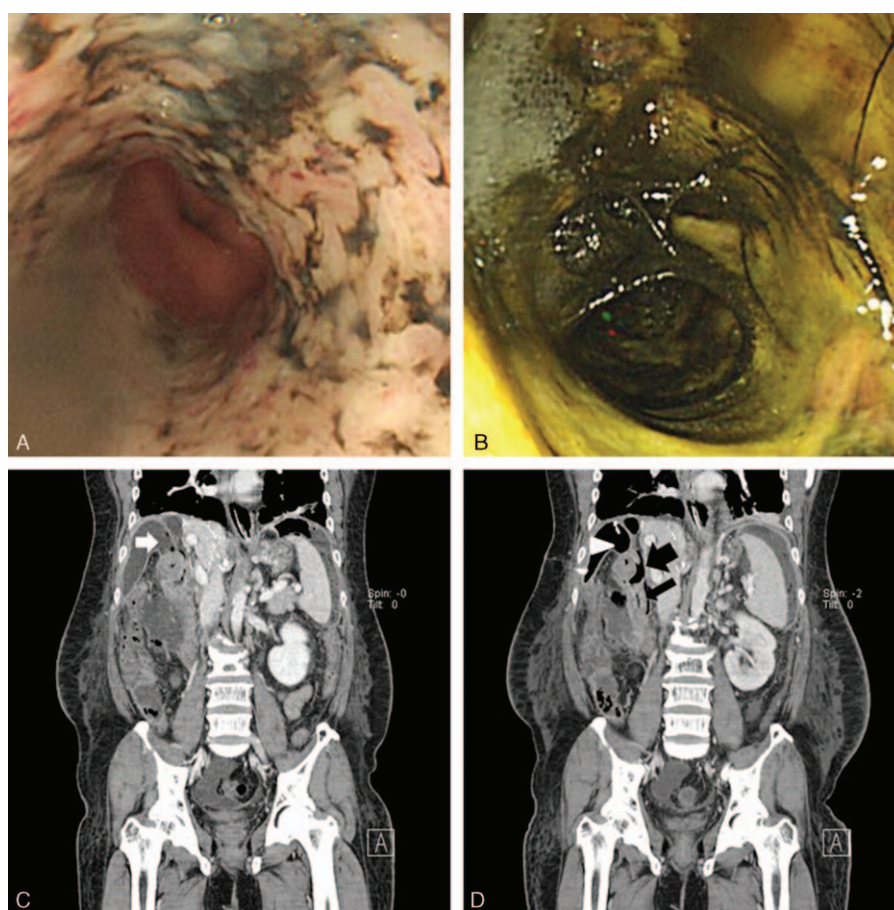


Figure 2. Esophagogastroduodenoscopy revealed necrotic tissue on lower esophagus (A) and necrotic tissue from bulb to distal area of duodenum (B). Abdominal pelvic CT (APCT) showed pneumoperitoneum with air containing fluid collection (white arrow) around duodenal bulb and left subphrenic space (C). Follow-up APCT on 4 days later after initial APCT revealed decreased size of some abscess pocket (white arrow head) with PCD insertion and slightly improved duodenal wall edema (thin black arrow), but no change of perforation size (thick black arrow) of duodenum (D). APCT = abdominal pelvic computed tomography, PCD = percutaneous drain.

the early detection of perforated free-air in the subphrenic area using simple x-ray. Furthermore, due to patient's hunger sensation, stable vital sign, and maintenance of nearly normoactive bowel sound, early diagnosis of mucosal necrosis in duodenum and esophageal necrosis combined with duodenal perforation was difficult before examination with EGD and APCT.

In terms of duodenal ischemia, it could not be suspected until the examination of EGD and APCT in this case due to the fact that duodenum is dually blood supplied from gastroduodenal artery and pancreaticoduodenal artery. Several mechanisms can explain this rare complication. First of all, the reflux of gel-form from proper hepatic artery into the gastroduodenal artery may be the cause. However, intact blood supply from pancreaticoduodenal artery to duodenum may prevent from complete necrosis of duodenal wall. Furthermore, it may result in complete recovery of potentially partial duodenal necrosis, which was confirmed in operative findings. Second, incorrect cannulation of guide-wire, although not intended, might have caused transient gel-form embolization in gastroduodenal artery. Also, repeated TACEs may have caused obliteration of peripheral hepatic arteries and previous abdominal operation also may have induced the collateral circulation.^[10] However, in this case, intervention radiologist has 15 years of experience for

TACE, and he had already recognized anatomical changes in advance through the previous 7 times of the TACE. Therefore, this explanation is less convincing. Nonetheless, to avoid unexpected vascular complications after TACE, a thorough understanding of the congenital and acquired anatomic variations in the arterial anatomy around liver is always required, especially in patients with posthepatectomy or repeated TACE.^[11]

Although duodenal perforation following TACE has been reported,^[6,12] esophageal ischemia combined with the duodenal perforation after TACE has never been reported in the literature. Interestingly, in this case, simultaneous ischemia on lower esophagus with duodenal perforation was identified after TACE. Low esophageal ischemia seems to be also induced by unexpected reflux of gel-form from proper hepatic artery to esophageal branch of left gastric artery. However, esophagus receives numerous blood supplies directly from the aorta. Therefore, it cannot be usually happened, and ischemia would have been limited to the lower esophagus and it may have been mild in this case.

Several previous studies tried to define the incidence or etiology of acute necrotizing esophagitis.^[13,14] The estimated incidence of the disease was ~0.2%, but its etiology has not been known. Moreover, most common endoscopic finding was

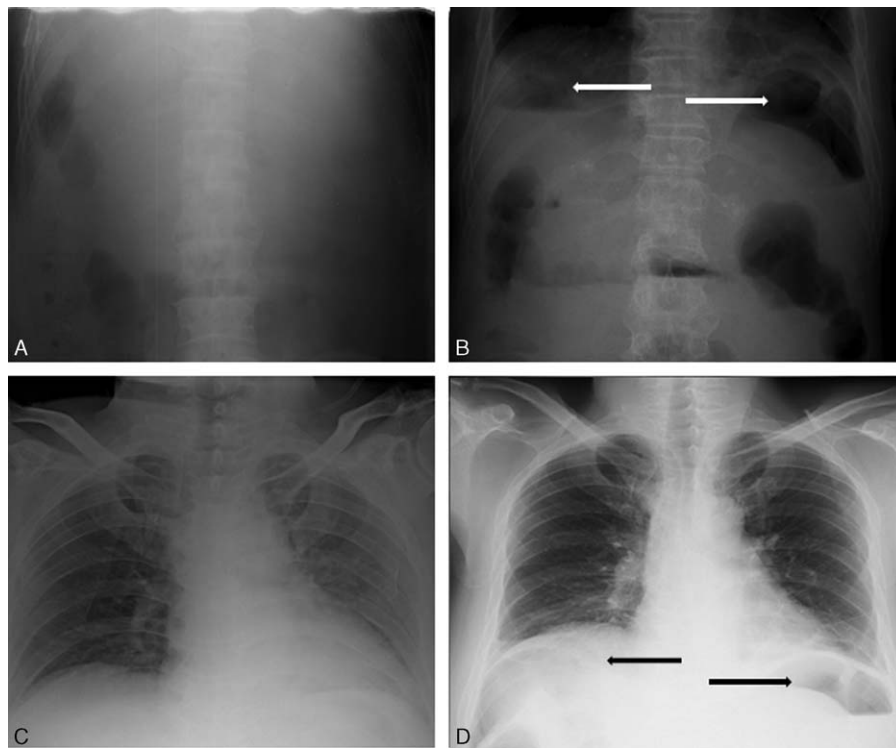


Figure 3. Simple abdomen and chest x-ray on the first day of TACE (A and C) and on the 3rd day after TACE (B and D). There was no intra-abdominal free air on baseline simple abdomen (A) and chest (C) x-ray. Intra-abdominal free-air (black and white arrow) was seen in the right and the left subphrenic area on simple abdomen (B) and chest (D) x-ray on the 3rd day after TACE. TACE = transarterial chemoembolization.

circumferential black discoloration in the distal esophagus extending to the proximal esophagus. In this case, this endoscopic finding was also observed, as shown in Fig. 2A. However, definite mechanism of esophageal ischemia was not documented in the present study, and this needs to be evaluated in the further studies.

In the present case, duodenal perforation seems to be caused by extensive duodenal wall necrosis or by stress-induced ulcer associated with TACE. Although EGD was not examined within 6 months of this event, EGD findings performed 1 year ago showed duodenal ulcer scar. Furthermore, underlying duodenal

ulcer might have been already present through 7 times of TACE. Although not intended, infused air during EGD may aggravate the size of the perforated duodenal mucosa.

In general, duodenal perforation should be immediately operated. In this case, if emergency surgery was performed right after detection of duodenal perforation, emergency Whipple operation or pylorus-preserving pancreaticoduodenectomy with gastrojejunostomy would have been required due to combined extensive duodenal ischemia. However, the authors decided not to perform emergency surgery with the expectation of improvement of duodenal ischemia. Furthermore, the surgery could be

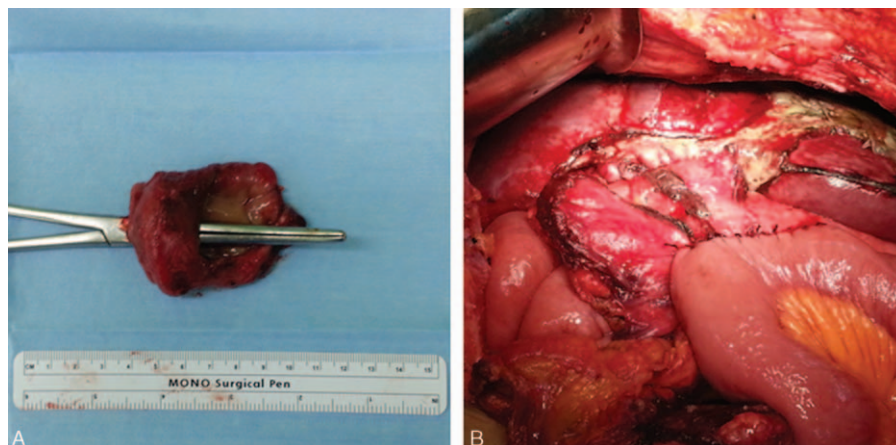


Figure 4. Full recovery of duodenal necrosis except perforation (A) allowed surgical repair to be simpler, just segmental duodenectomy (A) and gastrojejunostomy (B).

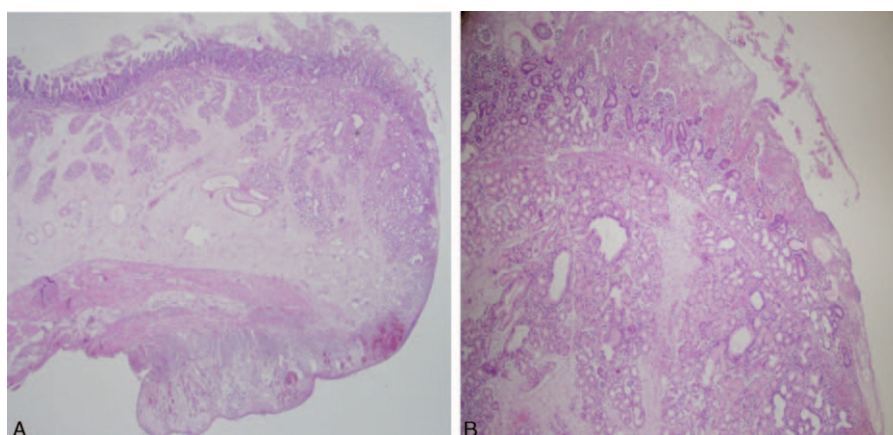


Figure 5. (A) Ruptured edge of duodenal wall shows abrupt discontinuity of muscle layer with granulation tissue formation, mucosal necrosis and subserosal inflammation, and hemorrhage (H&E, $\times 12.5$). (B) Adjacent mucosa of rupture site shows fibrinoid necrosis with disruption surface epithelia (H&E, $\times 40$). H&E = hematoxylin and eosin.

waited because hemodynamic status of the patient was stable and the fact that duodenum is the dually blood supplied. As expected, follow-up APCT images 4 days later showed the recovery of duodenal wall edema, which suggested improvement of duodenal ischemia. Of course, EGD would have been required to identify whether esophageal ischemia was recovered at the time of surgery. However, author considered that following EGD could worsen duodenal perforation, and that repeat EGD would not contribute to the therapeutic management. For these reasons, following EGD was not performed before surgery. Finally, the improvement of duodenal necrosis allowed surgical repair to be simpler, respectively, by duodenectomy and gastrojejunostomy alone.

This case report showed that duodenal perforation with necrosis and esophageal ischemia can occur as a complication of TACE. Although this complication is rare and unexpected, it may result in severe sequelae requiring surgical repair. Therefore, the careful procedure during TACE followed by post-TACE careful monitoring is required in patients with post-hepatectomy or repeated TACE, especially in the case with unusual clinical manifestations.

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