Acute pancreatitis induced by transarterial chemoembolization: a single-center experience of over 1500 cases

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BACKGROUND: Acute pancreatitis is a relatively rare but potentially lethal complication after transarterial chemotherapy. This study aimed to review the complications such as acute pancreatitis after transarterial chemotherapy with or without embolization for hepatocellular carcinoma.

METHODS: A total of 1632 patients with hepatocellular carcinoma who had undergone transarterial chemoembolization from January 2000 to February 2014 in a single-center were reviewed retrospectively. We investigated the potential complications of transarterial chemoembolization, such as acute pancreatitis and acute pancreatitis-related complications.

RESULTS: Of the 1632 patients with hepatocellular carcinoma who had undergone 5434 transarterial chemoembolizations, 1328 were male and 304 female. The median age of these patients was 61 years. Most (79.6%) of the patients suffered from HBV-related hepatocellular carcinoma. The median tumor size was 5.2 cm. Of the 1632 patients, 145 patients underwent transarterial chemoembolization with doxorubicin eluting bead, making up a total of 538 episodes. The remaining patients underwent transarterial chemoembolization with cisplatin. Seven (0.4%) patients suffered from acute pancreatitis post-chemoembolization. Six patients had chemoembolization with doxorubicin and one had chemoembolization with cisplatin. Patients who received doxorubicin eluting bead had a higher risk of acute pancreatitis [6/145 (4.1%) vs 1/1487 (0.1%), *P*<0.0001]. Two patients had anatomical arterial variations. Four patients developed acute pancreatitis-related complications including necrotizing pancreatitis (*n*=3) and pseudocyst formation (*n*=1). All of the 4 patients resolved after the use of antibiotics and other conservative treatment. Three patients had further transarterial chemoembolization without any complication.

CONCLUSIONS: Acute pancreatitis after transarterial chemoembolization could result in serious complications, especially after treatment with doxorubicin eluting bead. Continuation of current treatment with transarterial chemoembolization after acute pancreatitis is feasible providing the initial attack is completely resolved.

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KEY WORDS: transarterial chemoembolization; acute pancreatitis; hepatocellular carcinoma

Introduction

Transarterial chemotherapy with or without embolization (TACE) is commonly used in the treatment of primary hepatocellular carcinoma (HCC) or secondary liver cancers.[1-9] It is also used in neo-adjuvant or adjuvant setting in liver resection, or before liver transplantation to serve as a bridging therapy. It exploits the predominant hepatic artery blood supply of liver tumors to deliver a high dose of cytotoxic agents.[10, 11]

Acute pancreatitis (AP) is a rare but certainly well-known complication after TACE, which usually develops within 24 hours of the procedure. It occurs in around 1.7%-2% of all patients after selective and superselective liver embolization.[12] The potential morbidity and mortality of this iatrogenic AP cannot be overlooked especially in patients who suffer from underlying malignancy. The aim of this study was to review our experience in the management of patients who suffered from AP post-TACE.

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Methods

Patient selection

All patients with HCC who had undergone TACE during the period of January 2000 to February 2014 were reviewed retrospectively. The clinical, biochemical and pathological data of the patients were collected from our database.

Diagnosis of HCC

The diagnostic criteria for HCC in our center were as follows: 1) typical image abnormality with arterial enhancement and contrast washout in the portal venous phase in contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) or combined modalities; and/or 2) elevated serum AFP level >400 ng/mL. Needle biopsy was generally avoided in resectable or transplantable cases so as to avoid the risk of needle tract seeding of tumor cells. In resectable or transplantable cases, the diagnosis of HCC was confirmed histologically.[13]

Inclusion and exclusion criteria

The inclusion criteria for TACE for patients with HCC were as follows: unresectable HCC due to bilobar involvement or inadequate future liver remnant despite portal vein embolization, adjuvant therapy for unfavorable tumor pathology, high perioperative risk for surgery, recurrent HCC, and patient's preference. These patients might have undergone one or more episodes of TACE. For those patients who were diagnosed to have main portal vein thrombosis, ascites, poor liver function (Child's C cirrhosis, serum bilirubin level >50 μmol/L), poor renal function (serum creatinine >150 μmol/L), significant arterioportal venous shunting would be contraindicated for TACE.

Patients with incomplete laboratory tests before and after TACE, as well as those who suffered from chronic pancreatitis and recurrent pancreatitis unrelated to TACE were excluded.

Definition of AP

Diagnosis of AP was made according to the latest Atlanta classification 2012. It included two of the following three features: abdominal pain suggestive strongly of AP, serum amylase and/or lipase activity at least 3 times greater than the upper limit of normal and the characteristic findings of AP on transabdominal ultrasonography or on CT scan.[14]

AP after TACE

Post-TACE AP is defined as the onset of AP within 24 hours after TACE and the exclusion of other possible etiologies, such as alcoholism, gallstone disease, hyperlipidemia or hypercalcemia.

TACE procedure

Patients were fasted at six hours before TACE and adequate hydration was ensured by intravenous fluid. Blood tests including complete blood picture, liver and renal function test, amylase, clotting profile and AFP were taken for pre-procedural assessment. One dose of intravenous amoxicillin-clavulanic acid (1.2 mg) and pantoprazole (40 mg) were given at the time of transferal to the procedure. Vascular access was established via puncture of the femoral artery under local anesthesia. Hepatic and superior mesenteric angiographies were performed to define the size and locations of tumor nodules. The right or left hepatic artery feeding the tumor was superselectively catheterized. An emulsion was prepared by mixing cisplatin (1 mg/mL) with lipiodol in a volume ratio of 1 to 1. Various amounts of the emulsion, up to a maximum of 60 mL (containing 30 mg of cisplatin) were injected slowly under fluoroscopic monitoring according to the size of the tumor and until sluggish arterial flow was evident. For doxorubicin eluting bead (DEB), the usual dosage was 40-60 mg/m^2 with a maximum dosage of 150 mg for a single session. If the tumor involved both lobes of the liver or if superselective catheterization was not possible, the emulsion was injected into the proper hepatic artery distal to the origin of the gastroduodenal artery. This was followed by embolization with small gelatin-sponge (Spongostan; Ferrosan, Johnson & Johnson Medical Ltd., Skipton, England) pellets of 1 mm diameter mixed with 40 mg of gentamicin. After the procedure, oral amoxicillin-clavulanic acid (375 mg 3 times per day) and pantoprazole (40 mg per day) were administered for 3 days. Discharge from the hospital was decided according to the clinical state. Chemoembolization was repeated every 2 to 3 months and would be withheld or discontinued whenever vascular contraindications, poor liver function (bilirubin >50 μmol/L, presence of ascites), poor renal function (serum creatinine >150 μmol/L), severe adverse effects, or progressive disease developed.

Definition of vascular variations at the celiac trunk

Vascular anatomical variant of the celiac trunk was identified if there was presence of the replaced or accessory hepatic artery, common hepatic artery arising from the superior mesenteric artery or an early bifurcation of the celiac trunk.

Post-TACE management

Patients were fasted for at least four hours after the procedure and diet was resumed when tolerated. Abdominal, groin and peripheral vascular examinations were carried out to look for potential complications. Complete blood count, liver and renal function test,