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Case Report

Miriplatin-induced Acute Pancreatitis : A Case Report

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ABSTRACT

An 85-year-old man with alcohol-related hepatitis and hepatocellular carcinoma was admitted for transhepatic arterial infusion (TAI) using miriplatin without embolization. Acute pancreatitis developed 3 days after TAI. The patient recovered satisfactorily with conservative management of acute pancreatitis and was discharged 15 days after TAI. Acute pancreatitis is a rare complication of TAI, and miriplatin-induced acute pancreatitis has not been previously reported. We herein present such a case.

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Key words : hepatocellular carcinoma, transhepatic arterial infusion, acute pancreatitis

INTRODUCTION

Hepatocellular carcinoma (HCC) is the fifth most common malignancy in the world[1]. Because HCC is usually diagnosed at an advanced stage, curative therapies, including surgery, is applicable to only 30% to 40% of patients[2]. The blood supply in classic cases of HCC is dependent on the hepatic artery ; therefore, transcatheter arterial chemoembolization (TACE) and transhepatic arterial infusion (TAI) are used as effective palliative treatments for HCC. A rare complication of TAI is acute pancreatitis. We herein report on a patient with HCC in whom acute pancreatitis developed after TAI with miriplatin.

CASE REPORT

An 85-year-old man with alcohol-related hepatitis and chronic renal failure was found to have a large, solitary HCC in the right lobe of the liver. The patient had a history of hypertension, dyslipidemia, hyperuricemia, diabetes, and myocardial infarction. He had never had pancreatitis. Computed tomography (CT) showed an 8-cm HCC located in segment VIII and close to both right and middle hepatic veins with thrombus in the right branch of portal vein (stage T3N0M0, as defined by the 6th edition of the *General Rules for the Clinical and Pathological Study of Primary Liver Cancer* published by the Liver Cancer Study Group of Japan) (Fig. 1). Liver function was classified as Child-Pugh A, and the indocyanine green retention rate after 15 minutes was 19% (liver damage B). In view of the patient's age, liver function, and the location of the HCC, we decided to perform TAI with selective catheterization of the right hepatic artery (A8) from the common hepatic artery using a mixture of a cytotoxic agent (miriplatin, 70 mg) and lipiodol (4 ml) (Fig. 2).

Three days after TAI, the patient complained of fever and epigastralgia, and laboratory examination showed increased levels of serum pancreatic amylase (1,778 IU/lL)

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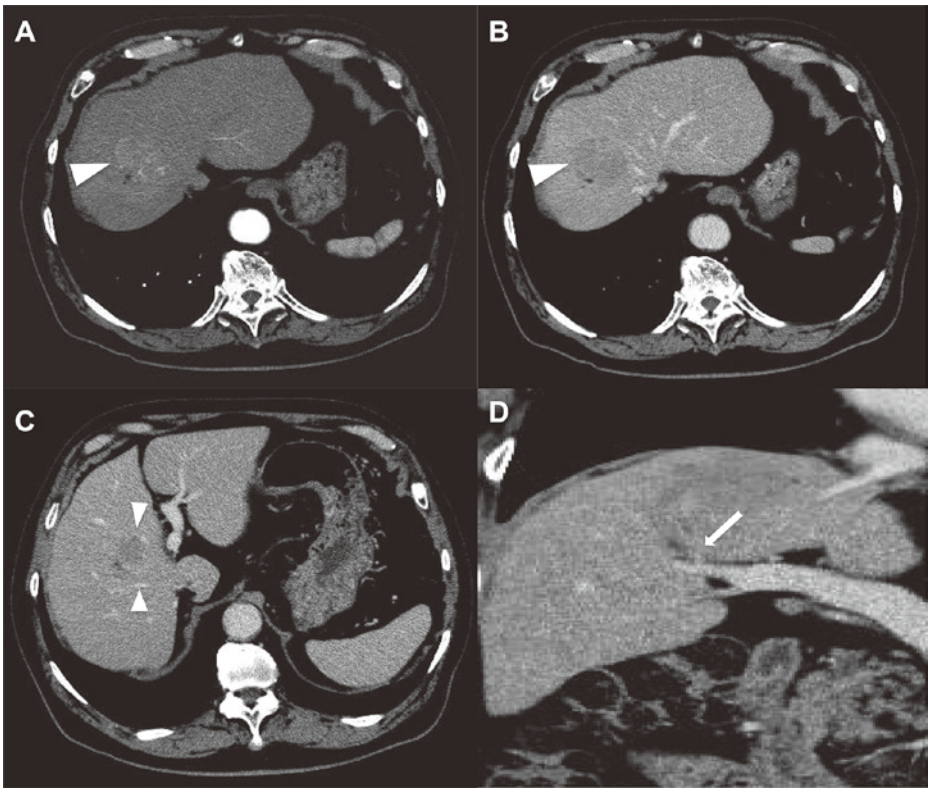

Fig. 1. Computed tomography of the abdomen showed an 8-cm hepatocellular carcinoma (A, B : arrowheads) located in segment VIII close to both the right and middle hepatic veins (C : arrowheads) with a thrombus in the right branch of the portal vein (D : arrow).

and C-reactive protein (1.22 mg/dL). Abdominal CT revealed swelling of the pancreas and peripancreatic fluid collection (Fig. 3). The prognostic factor score in the Japanese severity criteria for severe acute pancreatitis was 1 (age $\geq$ 70 years).

The acute pancreatitis was treated with conservative management : pain control, hydration, and fasting. The patient's symptoms and laboratory results improved without complications. He was discharged 15 days after TAI (Fig. 4).

Discussion

Acute pancreatitis is a rare but potentially lethal complication of transarterial chemotherapy. A study of 1,632 patients with HCC who had undergone TACE found that acute pancreatitis developed in 7 patients (0.4%), of whom 6 had chemoembolization with doxorubicin and 1 had chemoembolization with cisplatin[3]. Reported adverse effects of TAI with miriplatin include fever, anorexia, nausea, abdominal pain, leukopenia, neutropenia, anemia, thrombocytopenia, and increased levels of aspartate transaminase, alanine aminotransferase, total bilirubin, creatinine, and hypoalbuminemia[4]. However, to our knowledge, acute pancreatitis due to TAI with miriplatin has not previously been reported.

As a treatment for HCC, TACE can lead to several complications, including postembolization syndrome, fever, intrahepatic biloma, and cholecystitis. The incidence of acute pancreatitis after TACE has been reported to range from 1.7% and 4%[5]. A risk factor associated with acute pancreatitis after TACE is nonselected angiography, and TACE performed via the proper hepatic artery without selective catheterization to the tumor feeder vessels is reportedly associated with hyperamylasemia in approximately 40% of patients[6]. In the present patient, TAI, which is defined as injection of a chemotherapeutic agent without embolization, was selectively performed via the right hepatic artery A8. The patient did not receive any other new therapeutic agent or ingest alcohol during hospitalization. In addition, CT showed no gallstones or pancreatic arteriovenous malfor-

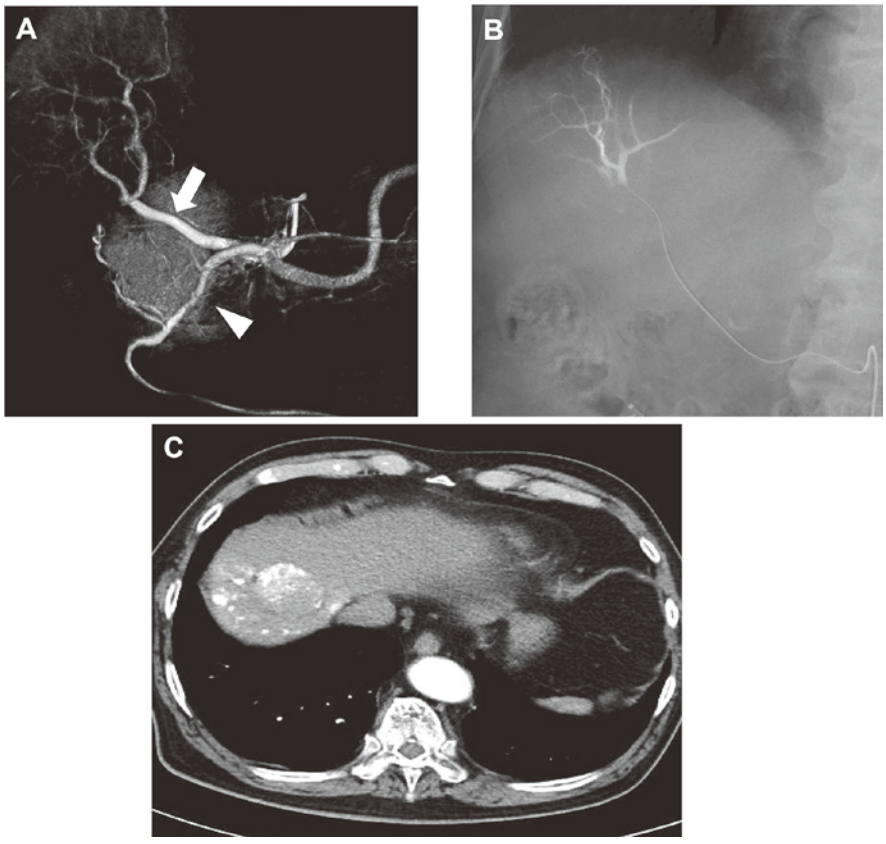

Fig. 2. Transhepatic arterial infusion was performed with selective catheterization (B) of the right hepatic artery (A8) feeding the tumor with a mixture of a cytotoxic agent (miriplatin, 70 mg) and lipiodol (4 ml) (A : proper hepatic artery ; arrow, gastroduodenal artery ; arrowhead).

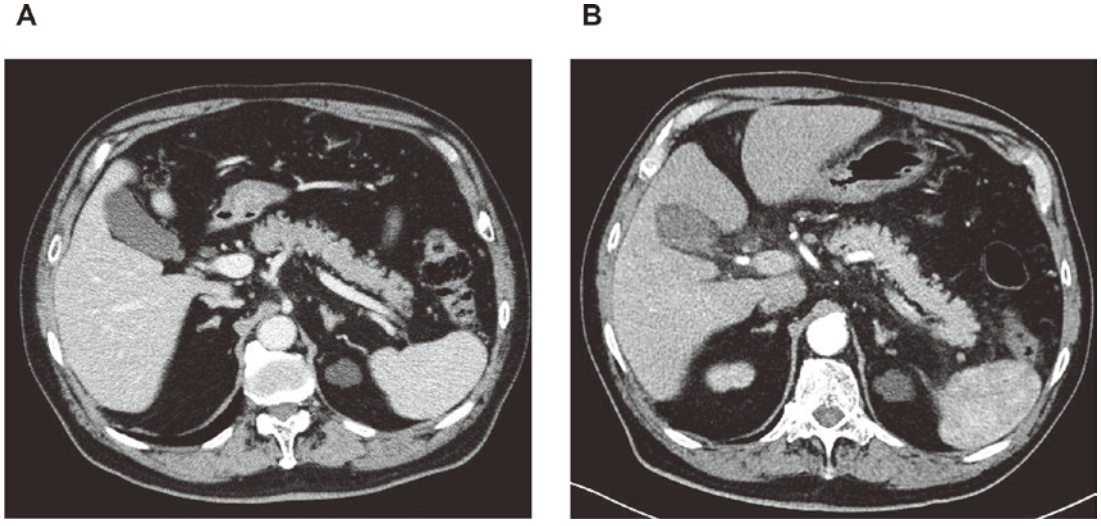

Fig. 3. Computed tomography of the abdomen demonstrated an irregular outline of the pancreas and a peripancreatic fluid collection (before [A] and after [B] transhepatic arterial infusion).

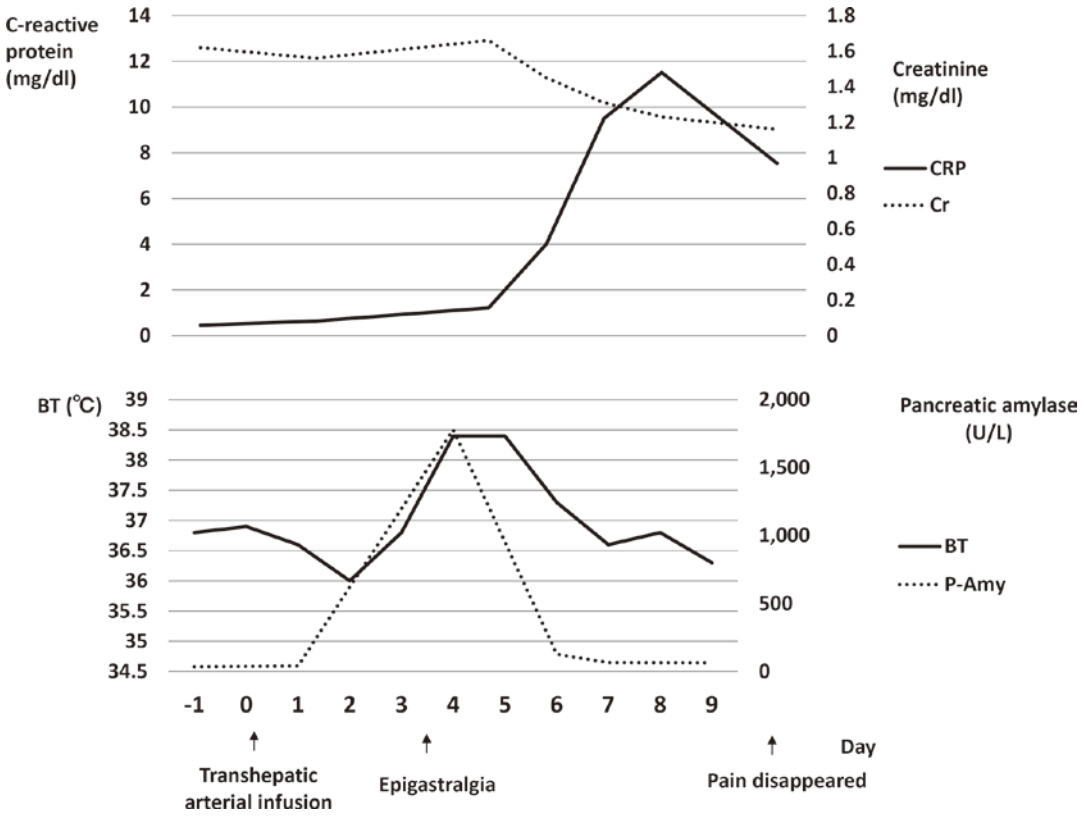

Fig. 4. The patient's clinical course. BT, total bilirubin.

mation, which can cause pancreatitis. Therefore, the acute pancreatitis was considered to be due to miriplatin.

Drug-induced pancreatitis is uncommon, and several drugs are listed in the World Health Organization database as suspected causes of the adverse effect of pancreatitis[7]. Several cases of pancreatitis induced by antineoplastic agents have been reported[8-10]; however, the mechanism of chemotherapy-induced pancreatitis remains unclear.

In conclusion, the present case of acute pancreatitis after TAI with miriplatin for HCC is, to our knowledge, the first to be reported. Acute pancreatitis after TAI is uncommon, but serum pancreatic enzymes should be monitored after TAI with miriplatin.

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