

Acute Pancreatitis and Cholangitis Caused by Hemobilia Secondary to Hepatocellular Carcinoma: A Case Report

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Abstract

A 60-year-old female had the history of cirrhosis of liver, Child's B, hepatitis B virus (HBV) related and hepatocellular carcinoma (HCC) [Tumor, Node, Metastasis (TNM) stage II, T2N0M0 and Barcelona Clinic Liver Cancer (BCLC) stage B post transcatheter arterial embolization (TAE) treatment]. She was sent to our hospital due to epigastric dull pain for 4 days and jaundice. Laboratory data disclosed elevations of pancreatic enzymes and total bilirubin level. Abdominal computerized tomography showed a tumor at segment 4 of liver (S4) with invasion of the common hepatic duct, which caused bilateral intrahepatic duct dilatation and extensive blood clots in the common bile duct, gallbladder and left intrahepatic duct. Mild pancreatic ductal dilatation was also noted. Acute pancreatitis and cholangitis related to hemobilia was considered. Due to poor liver function and high risk for TAE or surgery, the patient's family decided to receive supportive care. Hepatocellular carcinoma with bile duct invasion and homobilia is rare. Hemobilia typically presents with a triad of jaundice, biliary colic and gastrointestinal bleeding. Blood clot in biliary tract can cause cholecystitis and cholangitis. In addition, pancreatitis may also happen when blood clot enters the pancreatic duct incidentally. TAE is the recommended treatment for hemobilia. On the other hand, hepatectomy is not feasible for patients with advanced tumor of liver. (*J Intern Med Taiwan* 2013; 24: 500-504)

Key Words: HCC, Hemobilia, Jaundice, Acute pancreatitis, TAE

Introduction

Hepatocellular carcinoma (HCC) and cirrhosis of liver is highly prevalent in Asia-Pacific area.^{1,5} Patients usually present with advanced diseases of painful and huge mass in the right upper quadrant of the abdomen if not regularly follow-up.¹ However, obstructive jaundice is not commonly

seen. Bile duct invasion and portal vein thrombosis formation have been reported in patients with advanced HCC^{7,8,10}. Hemobilia is a kind of upper gastrointestinal bleeding caused by the communication between blood vessels and the biliary tract that results in bleeding through the duodenal papilla. In addition, icteric-type HCC is the condition due to tumor invasion into the bile duct causing progressive

obstructive jaundice, sometimes may associate with hemobilia.^{1,5,10} A large volume of hemobilia may cause acute pancreatitis. Both computerized tomography (CT) and endoscopic retrograde cholangiography (ERC) are useful in the diagnosis of hemobilia and localization of the bleeding sites. Selective TAE is effective for the treatment of advanced HCC that has ruptured into the biliary system and causes hemobilia.⁸

Case report

A 60-year-old female had the history of (1). Adenocarcinoma of lung, LUL with left pleural seeding, brain and lung to lung metastases, TNM stage IV (T4N2M1), under Iressa use (2). HCC, TNM stage II (T2N0M0, BCLC stage B) post TAE (3). Cirrhosis of liver, Child B, HBV related.

She had suffered from epigastric dull pain for 4 days. No radiation pain was noted. The pain was not related to meal or postural change. In addition, yellowish skin discoloration, tea-colored urine and vomiting were noted. She denied itchy skin, coffee ground vomitus, passage of tarry stool, bowel habit change, fever, chills or dysuria. She was sent to our ER and the vital signs showed as follows: BP: 123/54 mmHg, PR: 86 bpm, RR: 18 cpm, BT: 37.1°C. Physical examination revealed icteric sclera, mild tenderness over epigastric area without muscle guarding or rebounding tenderness. The laboratory data disclosed the following values: platelet: 65000/cumm (normal range: 150,000-400,000/cumm), PT: 14.7 sec (control: 10.4 sec), PT I.N.R.: 1.43 (normal range: 1.00-1.25), aPTT: 34.3 sec (control: 27.6 sec), amylase: 873 U/L (normal range: 30-110 U/L), lipase: 8843 U/L (normal range: 20-300 U/L), GPT: 95 U/L (normal range: 0-40 U/L), ALP: 310 U/L (normal range: 42-128 U/L), γ -GT: 463 U/L (normal range: 4-51 U/L, female), and total bilirubin: 6.8 mg/dl (normal range: 0.2-1.6 mg/dl).

The esophagogastroduodenoscopy revealed gastric ulcer and chronic non-atrophic gastritis. But,

bleeding from papilla of Vater was not seen during the exam. The abdominal CT showed a post TAE viable tumor at S4 with invasion of the common hepatic duct (CBD), causing bilateral intrahepatic duct (IHD) dilatation. (Figure 1) Besides, extensive blood clots in the biliary tree including CBD, gallbladder and left IHD were also found. (Figure 2)

At emergency room, abdominal pain was relieved by fasting, but dropping of hemoglobin level from 10.2 g/dL to 8.4 g/dL was detected, so blood transfusion with 2 units of packed RBC was done. Due to suspicion of acute pancreatitis and acute cholangitis, she was admitted for further IV hydration with prophylactic antibiotics. Later,

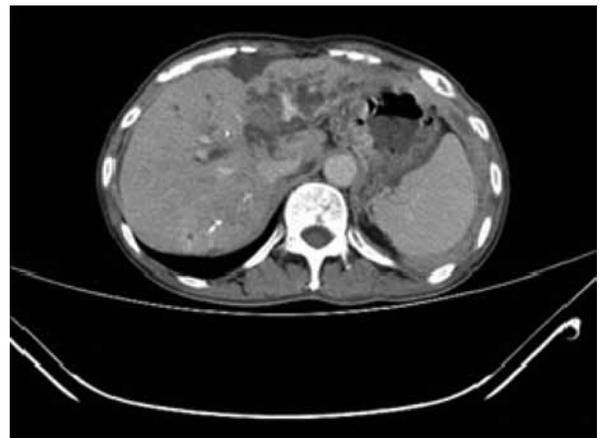


Figure 1. a viable tumor at S4 with invasion of the common hepatic duct (CBD), causing bilateral intrahepatic duct (IHD) dilatation.

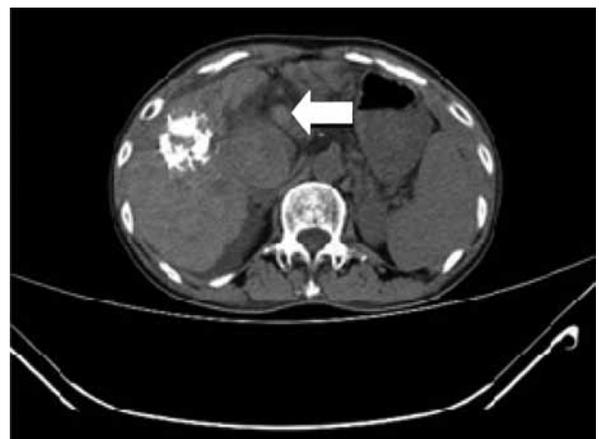


Figure 2. blood clots in the biliary tree including CBD (arrow), gallbladder and left IHD.

persistent obstructive jaundice with elevation of total bilirubin level up to 16.2 mg/dl was noted, and thus percutaneous transhepatic cholangio-drainage (PTCD) was performed, but the function of drainage was poor due to too much blood clot accumulation within the biliary tract. Endoscopic retrograde cholangiopancreatography (ERCP) or TAE was not done because of poor liver function and thrombocytopenia with bleeding tendency. Unfortunately, aspiration pneumonia and upper gastrointestinal bleeding developed, followed by drowsy consciousness, desaturation and shock. The patient's family decided to receive supportive care. Eventually, she expired under the DNR consent by her family.

Discussion

Icteric-type hepatoma is defined as the main extrahepatic bile duct is occluded either by tumor infiltration, tumor debris or blood clots which cause intermittent obstructive jaundice.^{1,5} Icteric-type hepatoma has been described in 1.2% of HCC patients in Taiwan and it is associated with complications such as cholangitis and hemobilia.⁵

Bile duct invasion and portal vein thrombosis have been reported rarely in patients with HCC, especially at advanced stage.^{7,8,10} Hemobilia is also a rare complication of HCC.¹² Hemobilia from bile duct tumor thrombi (BDT) could be massive and fatal.⁸ Hemobilia secondary to ruptured HCC is considered to be a terminal event leading to the rapid death of the patient due to the rarity of the condition and the consequent failure to recognize its presence.⁷ The symptoms have been reported to be abrupt abdominal pain, obstructive jaundice, melena and anemia,^{7,8,10-12} and hemobilia usually presents with a characteristic triad of jaundice, biliary colic and gastrointestinal bleeding.¹⁴

Hemobilia can occur with trauma, cholelithiasis, acalculous inflammatory disease, vascular conditions, neoplastic disease and surgery.^{1,4,11} HCC is more common as a cause for hemobilia

than hemangioma, cholangiocarcinoma, gallbladder carcinoma, adenocarcinoma of the pancreas, benign lesions in the bile ducts and gall bladder, and tumors metastasized to the liver or biliary tract.^{1,3,11}

Pancreatitis in hemobilia may occur due to obstruction of pancreatic duct.^{1,3} Reasonable explanation may be that the duct of Wirsung is intermittently occluded by the shedding tumor debris and blood clots.⁵ Hemobilia, with blood clots in the biliary tract and probable reflux into the pancreatic duct, could cause pancreatitis, cholestasis and cholecystitis.^{1,3,4} A large volume of hemobilia may cause acute pancreatitis if the rate of bleeding exceeds the intrinsic fibrinolytic capacity of the bile, and the mechanism is analogous to gallstone pancreatitis.^{4,13}

Because liver function deteriorates after the onset of hemobilia, early and accurate diagnosis is essential.¹⁰ Middle age, male sex, a history of hepatitis B or C, new-onset fluctuating jaundice accompanied by tarry stool passage, elevated level of AFP, and significant imaging findings of ultrasound (US) and computed tomography (CT), taken together, promote the suggestion of icteric hepatoma.⁵

Definitive diagnosis can be made by esophagogastroduodenoscopy, which confirms bleeding from the duodenal papilla.¹¹ Angiography is the gold standard for the diagnosis of persistent and recurrent hemobilia.¹⁴ but, it often fails to demonstrate the site of bleeding because of the intermittent nature and the variable rate of the bleeding.¹ If active hemorrhage accompanied by worsening of anemia is suspected, abdominal angiography is suggested to selectively image the hepatic artery.¹¹

CT and direct cholangiography, either endoscopic retrograde cholangiography (ERC) or percutaneous transhepatic cholangiography (PTC), are also useful in diagnosing hemobilia and localizing the bleeding sites. CT shows the presence of a high-density substance in the biliary tract, which is considered to be thrombus.⁷ The characteristic cholangiographic feature of bile duct involvement

by ruptured HCC is an intraluminal filling defect with irregular or lobulated outline and ground-glass radiolucency of the filling defects, which are considered to be thrombus or tumor debris.^{5,7}

Ultrasound examination is an ideal screening method by demonstrating the hepatic tumor and tumor debris within the common bile duct, but distinguishing icteric hepatoma and cholangiocarcinoma is difficult.⁵

Treatment of hemobilia should be focused on two goals. First, the consequences of the biliary obstruction including the pancreatitis should be resolved by non-operative methods. This could be readily achieved by ERCP and sphincterotomy with balloon dilation or drainage. Second, the origin of the migrating tumor should be eradicated either by transcatheter arterial embolization or hepatic resection.^{4,5}

Endoscopic sphincterotomy (ES) with nasobiliary drainage to maintain the luminal patency or balloon extraction of choledochal clot should be performed for acute obstructive pancreatitis as a potential complication of hemobilia.^{2,6,14} If rebleeding occurs, ES can prevent recurrent pancreatitis by blood clot impaction at the ampulla.³

Transcatheter arterial embolization (TAE) is the recommended treatment for hemobilia caused by bile duct tumor thrombi associated with hepatocellular carcinoma, but recurrent bleeding is common in the presence of HCC.^{3,6,8-10} Even when the embolized tumor is well controlled, other tumors that are not embolized can cause hemobilia.¹⁰ Repeated embolization or surgical resection is sometimes necessary.³ Kitagawa et al. reports that repeated selective TAE is useful for controlling recurrent hemobilia and contributes to prolonging survival in patients without rapid tumor progression.¹⁰ If TAE fails to establish hemostasis, surgical therapy, such as hepatic artery ligation or hepatectomy, is required.¹¹ Traditionally, the treatment of choice is selective embolization at hepatic angiography.¹²

Subsegmental TAE should be performed, if feeding artery of the BDT is clearly detected.⁸ Poor liver function, especially, the presence of hyperbilirubinemia (> 3.0 mg/dl) and a high frequency of portal vein invasion is thought to be critical for TAE, because liver failure may occur.^{7,8,10} Takao et al. reports that TAE followed by microwave coagulation therapy (MCT) is a useful treatment for HCC with portal and biliary tumor thrombi that rupture into the biliary system.¹⁰

Transcatheter hepatic arterial chemoembolization (TACE) is also selectively performed in the arteries feeding the ruptured HCCs for intraperitoneal hemorrhage.⁷ Although selective TACE has a strong anticancer effect, it is sometimes difficult to achieve complete necrosis when tumors are large and multiple.⁷

In patients with difficult hemostasis, there are a few cases treated by placement of a covered metallic stent in the biliary tract, but it may cause cholangitis due to bile duct branch occlusion.^{4,11} One report states that a potent vasoconstrictor with orni-pressin can be instilled into the biliary tract during ERCP for life-threatening massive hemobilia.¹²

Although hepatectomy seems to be the effective treatment, most patients are not candidates for surgery because they have advanced HCC, i.e., severe liver cirrhosis, stage IV or associated with portal vein tumor thrombi.^{7,8,10,11}

The outcomes of patients with icteric-type HCC are poorer than those of patients without biliary invasion.¹⁰ As to our patient, acute pancreatitis and cholangitis were caused by hemobilia, but ERCP or TAE was not done due to poor liver function including hyperbilirubinemia and thrombocytopenia.

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肝細胞癌導致膽道出血所造成之急性胰臟炎及膽管炎： 一病例報告

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摘 要

我們報告一位六十歲女性，病史為B型肝炎相關性肝硬化及肝癌，曾接受TAE(經動脈肝臟腫瘤栓塞術)治療。病患因為上腹鈍痛及黃疸送醫，胰臟酵素及膽紅素皆升高。腹部電腦斷層顯示一S4腫瘤侵犯總肝管而造成雙側肝內膽管擴張，合併總膽管、膽囊及左側肝內膽管血塊。疑似膽道出血造成之急性胰臟炎及膽管炎。肝細胞癌侵犯膽管而造成膽道出血並不多見，膽道出血通常呈現三合徵象：黃疸、膽絞痛及胃腸道出血。膽管內的血塊可以造成膽囊炎及膽管炎。若是血塊意外進入胰管，可能發生胰臟炎。經動脈肝臟腫瘤栓塞術為建議之治療，對於晚期之肝腫瘤，肝切除並不適合。