Intraductal Forceps Biopsy of Icteric Hepatocellular Carcinoma after Percutaneous Transhepatic Biliary Drainage

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To determine the usefulness and effectiveness of percutaneous transhepatic intraductal biopsy for icteric type hepatocellular carcinoma (HCC).

Thirteen patients with chronic hepatitis and obstructive jaundice received percutaneous transhepatic biliary drainage (PTBD). Intraductal forceps biopsy was performed through the established percutaneous transhepatic tract 1 to 2 weeks later.

Adequate specimen for pathological diagnosis was obtained in all patients. Transient hemobilia occurred in all patients and minor complications such as low grade fever and pain were occasionally seen. No major complication was encountered.

Intraductal forceps biopsy after percutaneous transhepatic drainage is a safe and effective method for tissue confirmation of icteric HCC even in cases of bleeding tendency and presence of small amount of ascites.

Key words: Bile ducts obstruction; Biopsy; Hepatocellular carcinoma

Jaundice is a common late manifestation in patients with HCC because of advanced liver cirrhosis or substantial tumor infiltration of the liver parenchyma [1, 2]. Obstructive jaundice is a rare initial manifestation of HCC with reported incidence of 1.2-9% [2-5]. In 1975, Lin et al. reported 8 cases of HCC invading biliary tree at their early stage and named this specific HCC as an “icteric type hepatoma” [2]. Subsequently, sporadic cases of HCC with bile duct invasion have been reported. Kojiro et al. stated that intraductal growth of the neoplasm seems to be attributed in most case [3]. However, tissue proof of such neoplasm may be difficult because the primary tumor may be small and rupture into bile duct early in the disease process. Furthermore, a core needle biopsy is not always possible due to the presence of ascites and bleeding diathesis in the patients with liver cirrhosis. Relief of obstructive jaundice is mandatory for both preservation of normal liver function and control of cholangitis that can be achieved by PTBD. It will be ideal if PTBD can be used for relief of obstructive jaundice and existing percutaneous transhepatic tract provides a route for tissue confirmation. Intraductal biopsy of HCC has been rarely reported [6, 7] and no large scale study has been conducted. Thus, we reported our experience of intraductal forceps biopsy using the existing tract after PTBD for tissue proof in 13 patients.

PATIENTS AND METHODS

From March 2000 to September 2004, 13 chronic hepatitis carriers complicated with liver tumor and elevated bilirubin level (9.5 to 18.7 mg/dL, mean 13.6 mg/dL) as well as imaging diagnosis of obstructive jaundice were enrolled in this study. There are 12 male and 1 female patients with the ages ranging from 32 to 83 years and a mean of 56 years. The level of Alfa-fetoprotein (AFP) ranged from 8 to 256 (ng/ml). None of these patients had received any treatment before PTBD.
Bleeding diathesis resulting from thrombocytopenia (platelet < 50,000/ mm³) was found in 3 patients and prolonged prothrombin time in another 5 patients. Computer tomography (CT), magnetic resonance imaging (MRI) and Magnetic Resonance Cholangiopancreatography (MRCP) performed prior to PTBD revealed small amount of ascites at right subphrenic and/or subhepatic space in 6 patients.

Ultrasound-guided left-sided biliary drainage was successfully performed in all patients after blood product transfusion to correct the bleeding tendency. Puncture was done with 21-gauge needle (US Guided Puncture Needle, Cliny, Yokohama, Japan) and 0.018-inch guide wire (Radifocus Guide Wire, RF*GA18153M, Terumo, Tokyo, Japan) was inserted into the dilated ductal branch through the needle cannula. Advancement of the guide wire was monitored under fluoroscopy after opacification of the bile ducts with injection of contrast medium. Initially, an 8.5-French pigtail catheter (Nephrostomy Catheter, Cook, Bloomington, Indiana, USA) was placed proximal to the obstruction site for relief of the obstructive jaundice and cholangitis. After maturation of the PTBD tract and subsidence of the cholangitis within 1-2 weeks, a 0.035-inch guide wire (Radifocus, RF*GA35153M, Terumo, Tokyo, Japan) was used to cannulate through the obstruction and passed down into duodenum. A 6-French angiographic introducing sheath (Radifocus introducer II, Terumo, Tokyo, Japan) was used as a working channel.

**Figure 1.** Diagnostic cholangiography shows a large intraluminal filling defect in the CHD and CBD (arrows) and the “cupping” appearance of left hepatic duct (arrowheads).

**Figure 2.** Photograph of the biopsy forceps.

**Figure 3.** Biopsy is done with the biopsy forceps placed at the proximal (a) and distal (b) part of the intraluminal filling defect.
Intraductal biopsy of hepatocellular carcinoma

and placed just proximal to the obstruction site. A 4-French angiographic catheter (Radifocus, J curve, Terumo, Tokyo, Japan) was placed to distal CBD and slowly withdrawn with contrast medium injected from both sides of the obstruction for diagnostic cholangiography (Fig. 1). Then, a 5-French biopsy forceps (FB-19C, Olympus, Tokyo, Japan) (Fig. 2) was inserted into introducing sheath. The intraductal biopsies were performed at three different sites of the intraluminal filling defect (distal, middle and proximal portion, total 6 times) in each patient (Fig. 3) and the specimens were fixed with formalin for pathological examination. Finally, an 8-French straight drainage catheter (Cholangio Entero Tube, Cliny, Yokohama, Japan) with multiple side holes was placed crossing the obstruction for internal-external bile drainage (Fig 4). Broad-spectrum antibiotics before and after the procedure were routinely administrated and written informed consent was obtained from all patients before the PTBD and biopsy.

RESULTS

Diagnostic cholangiography showed obstruction involving common hepatic duct by intrinsic lesion in all 13 patients. A bulky oval or round intraluminal filling defect in the CHD was found in all patients. Non-opacification of right hepatic duct was found in 4 patients. The maximal diameter of the intraluminal filling defect ranged from 16 to 35 mm.

Adequate samples for histological diagnosis were obtained in all patients and all were proved to be HCC. Neither massive bleeding nor other major complications was noted after forceps biopsy in all patients despite transient hemobilia. The bloody bile became clear and drainage volume returned to normal within 24 hours. Transient low grade fever (< 38°C) with chills was found in 3 patients.

DISCUSSIONS

Direct cholangiographic features and magnetic resonance cholangiographic (MRC) appearances of icteric HCC have been reported previously [8-10]. Although the typical cholangiographic features suggest icteric HCC, the differential diagnosis should include malignant tumor of bile duct, gallbladder and pancreas, with or without hemobilia. Despite the recent advance in imaging modalities, icteric type HCC is frequently misinterpreted as cholangiocellular carcinoma or choledocholithiasis clinically [2, 4, 8, 9], partly because of their similar symptoms and signs.

Pathological proof is important for these patients because the prognosis of icteric type HCC is extremely poor with median survival of 4.5 months or less if the patients are only treated palliatively [4]. Better prognosis has been reported for patients with resectable tumor, and excellent result has been reported sporadically [5]. Thus, it is important to find the patient who is eligible for curative surgery. Tissue proof of icteric type HCC may be difficult because the primary tumor may be small and the tumor may be mainly confined to the biliary tree. Furthermore, the presence of ascites and bleeding tendency due to liver cirrhosis may unwarrant biopsy in these patients.

Several techniques are currently available to perform biopsy for malignant obstructive lesions of bile duct. Intraductal biliary brushing cytology is an easy and safe method of obtaining cellular material when evaluating biliary malignancy, either endoscopically or percutaneously. Unfortunately, the results have been disappointing with a reported sensitivity of 30% to 53% [11-16]. When the biliary obstruction is caused by a small tumor, it is advocated that intraductal biopsy is a preferable method. It would be ideal that PTBD can be used for relief of obstructive and create a portal for biopsy at the same time.

In 1978, Palayew and Stein initially reported intraductal biopsy via a formed postoperative T-tube tract [17]. Nishimura et al. used a transhepatic access to introduce a 20-French choledochoscope and visually direct biopsy with 7-French bioptome [18]. However, the drawback of this method is that the tract must be dilated into a 16 Fr. Caliber in order to accommodate the cholangiofiberscope. This
increases the potential risk of bleeding and prolongs the waiting for treatment planning. Terasaki et al. used a 3-French or 5-French bioptome, originally designed for transjugular endomyocardial biopsies, for percutaneous transluminal biopsy of biliary strictures. In all 6 patients of their study, the histological diagnosis was positive for malignancy and correlated with the patient’s known primary tumor [19]. Tsai et al. performed percutaneous transhepatic biopsy for patients with obstructive jaundice by using a 9-French sheath with radiopaque band to accommodate a guide wire and forceps. The sensitivity was 71% and 3 out of their 16 patients had diagnosis of HCC with intrahepatic bile duct invasion.

The high positive rate of our biopsy could be attributed to sampling of the specimen from an intraluminal polypoid lesion rather than from a stenotic lesion. Moreover, a total of 6 biopsies was routinely taken from 3 different locations of the intraluminal filling defect in our series. A similar result with a sensitivity of 100% in 15 patients was obtained by taking 3 biopsies via percutaneous transhepatic cholangioscope [20].

No significant hemorrhage or bile leakage was found after biopsy in this study despite transient hemobilia is found early in the procedure in all patients. Contact bleeding easily occurred when we passed the guide wire across the intraluminal filling defect and advanced the introduce sheath against the tumor fragment. Transient hemobilia completely regressed in 24 hours in all patients. Transient low grade fever with chills was found in 3 patients and regressed in 24 hours in all patients. Transient hemobilia completely found after biopsy in this study despite transient.

In conclusion, our experience shows that intraductal forceps biopsy after PTBD is a safe and effective method for tissue diagnosis in case of icteric type HCC revealing characteristic cholangiography. Ultrasound-guided PTBD from left lobe approach can be used to relieve the obstructive jaundice even in patients with bleeding tendency with small amount of ascites. The established transhepatic tract can be used for intraductal biopsy without significant complications.

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經由經皮穿肝膽道引流術疊管在膽道內進行黃膽性肝癌切片

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本報告嘗試決定在有凝血功能障礙或有腹水的慢性肝炎病患的膽道內進行黃膽性肝癌切片的可行性及安全性。

經電腦斷層或磁振造影術疑因腫瘤造成膽道阻塞的十五名慢性肝炎病患，先接受經皮穿肝膽道引流術。待一至二週疊管成熟後，在疊管內進行腫瘤切片。

在所有十五名病患均能取得足夠且正確的標本以診斷為肝癌。所有的病患都曾有短暫的膽道出血，但均在二十四小時內恢復正常的膽汁流量及色澤。兩位病患曾發生短暫的輕微發燒。少數病患在切片時感短暫疼痛。但無任何重大的併發症發生。

在經皮穿肝膽道疊管內進行腫瘤切片是一項安全且可靠的檢查。對黃膽性肝癌的病人既可解決黃膽的問題又能獲得正確的病理組織。

關鍵詞：肝癌  切片  膽道引流