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# Adenosquamous Carcinoma of Extrahepatic Bile Duct: A Case Report

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Most malignant tumors originating from the biliary tract are adenocarcinomas, and adenosqamous carcinoma of Klatskin's tumor is a very rare finding. An 83-yr-old man was admitted to our hospital because of jaundice. The abdominal computed tomography and magnetic resonance cholangiopancreatography revealed wall thickening and luminal stenosis of both the intrahepatic duct confluent portion and the common hepatic duct. These findings were compatible with Klatskin's tumor, Bismuth type III. Considering the patient's old age, palliative combined modality therapy was performed. After percutaneous transhepatic biliary drainage, biopsy was performed via percutaneous transhepatic cholangioscopy. The histopathologic findings showed adenosquamous carcinoma. External radiotherapy and intraluminal brachytherapy through the endobiliary Y-type stent were then done. Nine months after the radiotherapy, the laboratory findings and the abdominal computed tomography revealed biliary obstruction and progressive hepatic metastasis. The combined modality therapy of external radiotherapy, intraluminal brachytherapy and stenting assisted him to live a normal life until he finally experienced biliary obstruction.

**Key Words :** Adenosquamous carcinoma, Klatskin's tumor, Brachytherapy

## INTRODUCTION

Primary carcinoma of the extrahepatic bile duct is a rare tumor that represents less than 1.0% of all malignant neoplasms and less than 3.0% of all the tumors of the gastrointestinal system[1]. Most malignant tumors generated in the biliary tract are adenocarcinomas, and adenosquamous carcinoma is rare (3.0~4.7%). Adenosquamous carcinoma consists of two malignant components: one is glandular and the other squamous[2, 3].

In one previous report on patients with extrahepatic adenosquamous carcinoma of the biliary tract, patients were treated with surgical resection. the overall 1-year, 3-year and 5-year survival rates were 57%, 26% and 16%, respectively, and the median survival was 13 months[2]. When used for the management of advanced cholangiocarcinoma, adjuvant external beam radiotherapy (EBRT) followed by surgical resection with or without intraluminal radiotherapy (ILRT) is feasible, but the effect of radio-therapy alone has not been established[4].

In Korea, adenosquamous carcinoma of the papilla of Vater and the liver has been reported, but there have been no previous reports on adenosquamous carcinoma of Klatskin's tumor[5, 6]. We report here on a case of a patient with adenosquamous carcinoma of Klatskin's tumor, and this was confirmed by endoscopic biopsy. The patient was palliatively treated by EBRT and ILRT via his stent.

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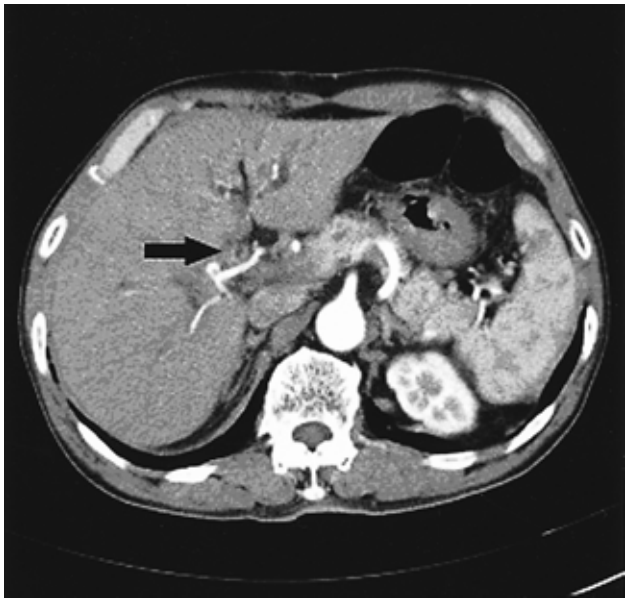
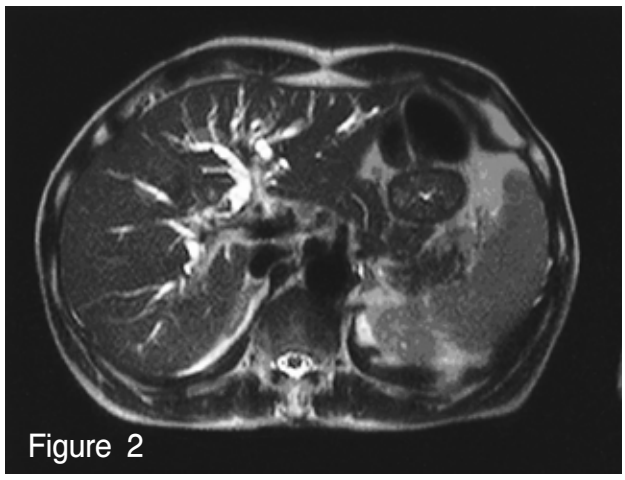


**Figure 1.** The abdominal computed tomography shows both intrahepatic duct dilatation and an enhanced wall thickening (arrow) of the intrahepatic duct confluent portion.



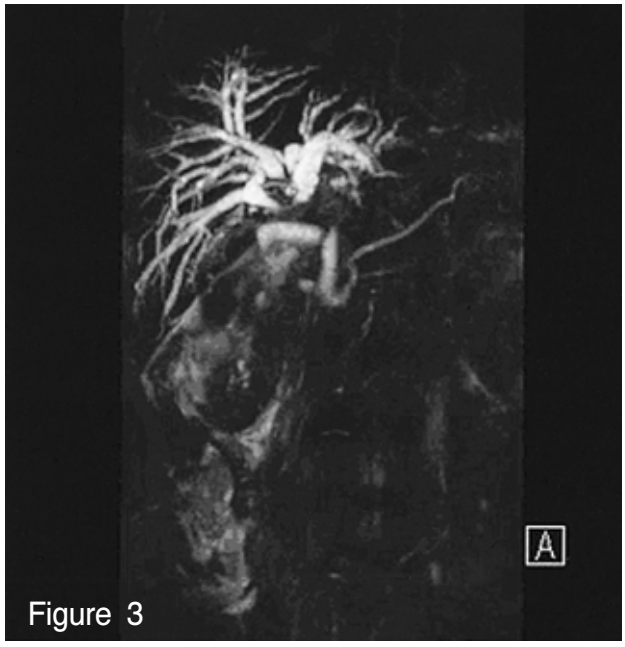




**Figure 2, 3.** The magnetic resonance cholangiopancreatography shows luminal stenosis of both the intrahepatic duct confluent portion and the common hepatic duct, and dilatation of both intrahepatic ducts.

## CASE REPORT

An 83-yr-old man was admitted to Eulji University Hospital because of jaundice he had experienced for the past 4 days, and this was preceded by chills and myalgia for the previous week. Ten years earlier, he had undergone percutaneous coronary intervention due to angina. Six months previously, he was operated on for laparascopic cholecystectomy due to acute acalculous cholecystitis with empyema.

On admission, his blood pressure was 100/60 mmHg, the heart rate was 66/min, the respiration rate was 20/min and the body temperature was 36.5℃. He looked acutely ill and showed an alert mentality. His sclera was icteric and he complained of abdominal pain. On physical examination, there was no abdominal tenderness, rebound tenderness or guarding of the abdomen. There was no palpable mass or hepatomegaly on the abdominal exam. On the biochemical analysis, the complete blood count was as follows: the white blood cell count was 9,740/μL, the hemoglobin level was 13.8 g/dL and the platelet count was 225,000/μL. The laboratory data included the following: total serum bilirubin: 11.5 mg/dL, serum glutamic oxaloacetic transaminase: 276 IU/L, serum glutamic pyruvic transaminase: 299 IU/L, alkaline phosphatase: 487 IU/L, serum gamma guanosine triphosphate: 640 IU/L, amylase: 64 U/L, lipase: 61 IU/L, alpha-fetoprotein: 5.1 ng/mL, carcinoembrionic antigen: 1.59 ng/mL and carbohydrate antigen 19-9: 120.62 U/mL.

The abdominal computed tomography (CT) revealed enhanced wall thickening of the intrahepatic duct (IHD), the confluent portion and the common hepatic duct (CHD), and this was all compatible with Klatskin's tumor. The CT also revealed enlarged lymphadenopathy of the portahepatis (Figure 1).

The magnetic resonance cholangiopancreatography (MRCP) revealed luminal stenosis of both the IHD confluent portion and the CHD, and dilatation of both IHDs. This was again compatible with Klatskin's tumor, Bismuth type IIIa (Figure 2, 3).

Considering his old age, palliative external radiotherapy and intraluminal brachytherapy were planned. After percutaneous transhepatic biliary drainage (PTBD) for achieving bile drainage, biopsy was performed via percutaneous transhepatic cholangioscopy (PTCS). An endobiliary Y-type stent was inserted via the

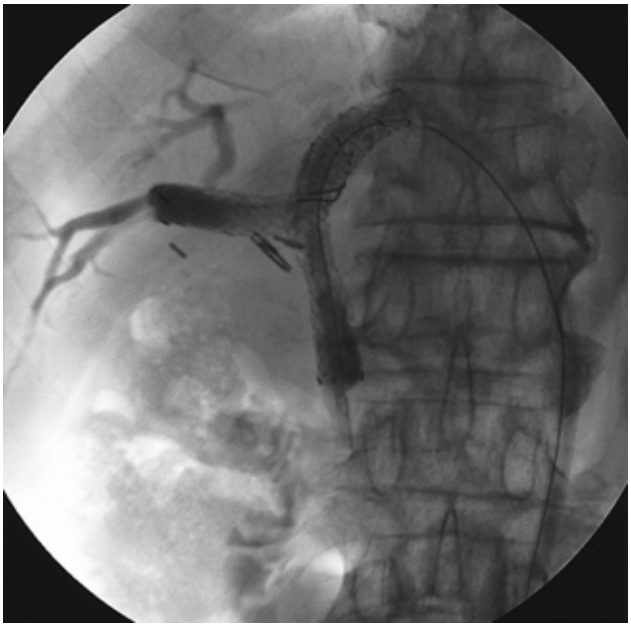


**Figure 4.** The endobiliary Y-type stent is inserted via percutaneous transhepatic biliary drainage of the left intrahepatic duct.

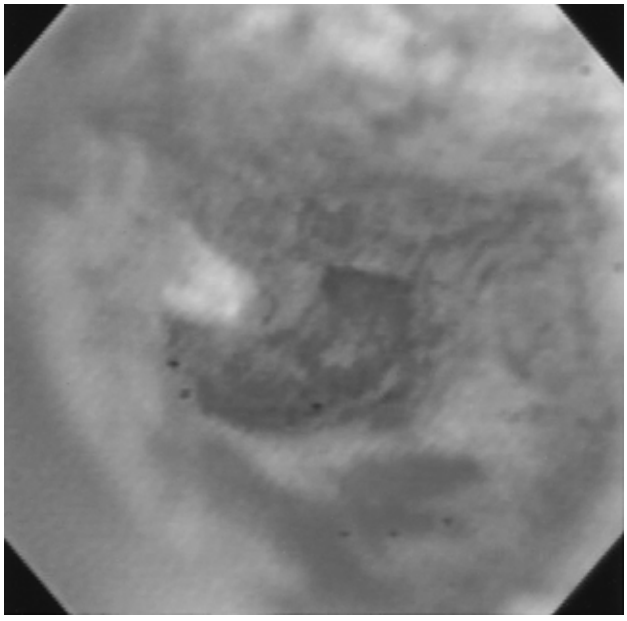


**Figure 5.** The percutaneous transhepatic cholangioscopy shows an ingrowing mass in the perihilar area.

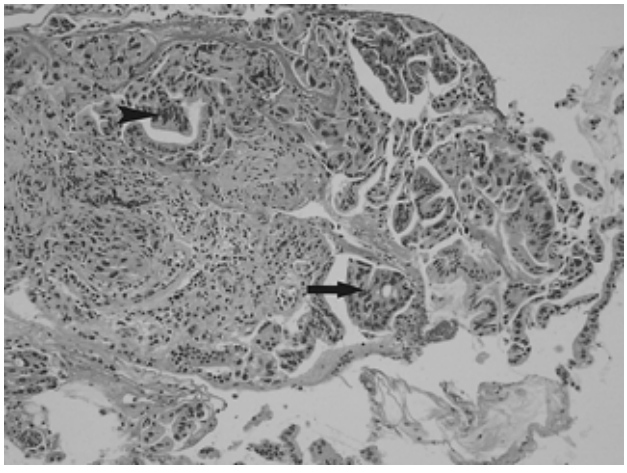


**Figure 6.** The light microscope findings show papillary structure (arrowhead) and proliferation of nests of adenocarcinoma cells (arrow) (HE stain, original magnification ×40).

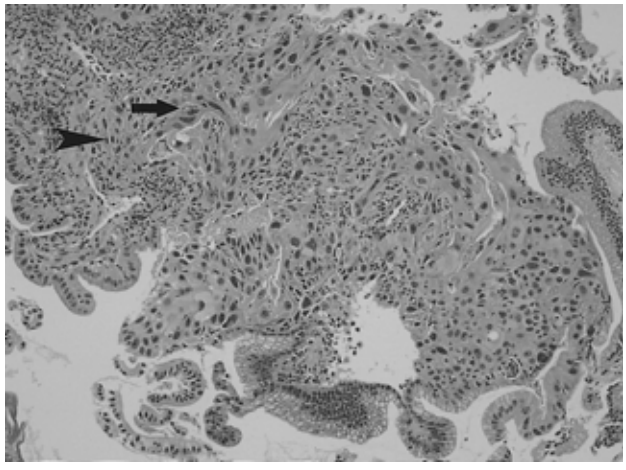


**Figure 7.** The light microscope findings show squamous cell carcinoma, including keratin (arrow) and intercelluar bridges (arrowhead) that are seen in the tumor tissue (HE stain, original magnification ×40).

PTBD of the left IHD (Figure 4, 5).

The histopathologic findings showed adenosquamous carcinoma that was a mix of adenocarcinoma and squamous cell carcinoma (Figure 6, 7).

External radiotherapy (22 cycles, total dose: 3,960 cGy) and intraluminal brachytherapy (2 cycles, total dose: 2,000 cGy) were performed through an endobiliary Y-type stent.

PTCS was performed one month after the radiotherapy. This revealed a dilated internal lumen by the endobiliary Y-type stent and superficial necrotized yellowish tissue on the tumor (Figure 8).

During the monthly follow-up nine months after the radiotherapy, the abdominal CT revealed biliary obstruction and progressive hepatic metastasis. PTBD was performed and conservative management was being planned.

## DISCUSSION

Most malignant tumors originating from the biliary tract are adenocarcinomas, but adenosqamous carcinoma is a rare

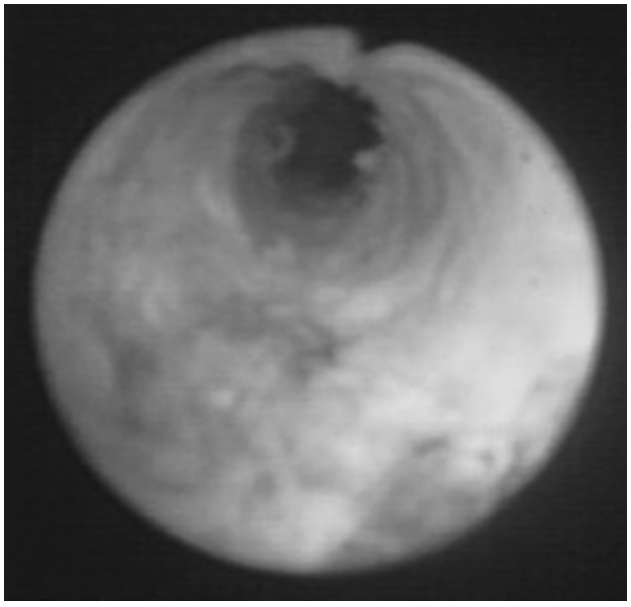


**Figure 8.** The percutaneous transhepatic cholangioscopy shows a dilated internal lumen via the endobiliary Y-type stent, and superficial necrotized yellowish tissue.

finding, representing less than 5% of all biliary tumors. Its clinical characteristics, pathogenesis and the effect of radiotherapy without surgical resection are unknown[1].

Several theories have explained that adenosquamous carcinoma is a mix of adenocarcinoma and squamous cell carcinoma, and this is a malignant epithelial tumor that's derived from initially benign metaplasia as a result of some chronic inflammatory process. Further, squamous cell carcinoma in these unusual sites is more likely to be due to squamous metaplasia of a tumor itself rather than being due to malignant transformation of previously benign metaplastic epithelium[1]. Histologic alteration from adenocarcinoma to squamous cell carcinoma shows that adeno-squamous carcinoma might be a transitional form from adenocarcinoma to squamous cell carcinoma. In addition, some of the primary hepatic squamous cell carcinomas might originate from adenocarcinomas, and this supports the theory of an origin from adenocarcinoma[7, 8].

Although adenosquamous carcinoma of the common bile duct has a different etiology and biologic features compared with adenocarcinoma, the patients with adenosquamous carcinoma are treated in the same manner as that for patients with adenocarcinoma. Adenosquamous carcinomas are uncommon tumors with a poor prognosis, even after surgical resection. The median survival is only thirteen months and no optimal postoperative adjuvant therapy has been established. The outcomes related to various therapeutic interventions are not well defined[2]. In one previous study on treating patients with inoperable carcinoma of the extrahepatic bile ducts, group 1 underwent EBRT alone and group 2 was treated with EBRT in combination with high-dose-rate ILBT; the results were then compared. No statistically significant difference was found in the recurrence rates between those who did and did not receive ILBT (53% for group 1 vs. 36% for group 2; $p$>0.05). However, a prolongation of the median time to tumor recurrence was observed for the group 2 patients (5 months for group 1 vs. 9 months for group 2; $p$=0.06)[9]. On the other hand, reports exist that performing brachytherapy boost was not superior to treatment with external beam irradiation alone[10]. In another study, there did not seem to be any difference in survival or complications between the low- and high-dose rate brachytherapy[11]. Moreover, high radiation doses could be dangerous and detrimental to the prognosis[10].

Takamura et al. reported that combined-modality therapy, including external beam radiotherapy, intraluminal irradiation and biliary stenting for extrahepatic bile duct carcinoma provided reasonable local control and improved the quality of life for the patients with extrahepatic bile duct carcinoma. The median survival was twelve months, with 1-, 3- and 5-year actuarial survival rates of 50%, 10% and 4%, respectively[12].

Therefore, the outcomes and survival rate related to radiotherapy have not been established for cases of inoperable extrahepatic bile duct carcinoma with obstructive jaundice. Yet it has been recently reported that ILBT with metallic stenting improves the quality of life of extrahepatic bile duct carcinoma patients with obstructive jaundice.

The reported mean time of stent patency was 421 days in the group of patient with proximal malignant biliary stricture and mean time of stent patency was 168 days for the group of patients with distal stricture that was impossible to operate on or the patients refused an operation[13]. So, we expected the period of stent patency to be more than six months for our case of adenosquamous carcinoma. We performed combined modality therapy of EBRT, ILRT and stenting. He lived a normal life until he experienced biliary obstruction. Nine months after the therapy, the abdominal CT and laboratory findings showed recurred biliary obstruction.

All the reported cases of adenosquamous carcinomas have been diagnosed by surgical resection. Any inoperable cases that were diagnosed by endoscopic biopsy have not yet been reported on because endoscopic biopsy is not generally performed before a treatment decision. Thus, the response to radiotherapy, including brachytherapy, and the patency rate of stents in inoperable adenosquamous carcinoma have not been reported.

In the future, a reasonable management plan for adeno-squamous carcinoma will be established if a sufficiently large number of cases of inoperable adeno-squamous carcinomas are diagnosed by endoscopic biopsy.

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