Case Report

Primary Squamous Cell Carcinoma of Extrahepatic Bile Duct Associated with Choledochal Cyst: A Case Report and Literature Review

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Extrahepatic bile duct malignancy is mostly an adenocarcinoma cell type. The squamous cell carcinoma is scarcely reported in the literature. The authors are presenting an interesting case of this rare tumor. A 36-year-old man with obstructive jaundice and epigastric pain was referred to the authors hospital. Blood tests showed direct hyperbilirubinemia and elevated ALP. Imaging studies demonstrated dilated bilateral intrahepatic bile ducts with disproportional fusiform dilatation of extrahepatic bile duct compatible with choledochal cyst type 1. There was also the abrupt narrowing of distal CBD associated with enhancement of irregular periductal soft tissue that suggested a malignant feature. After biliary drainage, the patient underwent pancreaticoduodenectomy with bile duct excision to remove the choledochal cyst and tumor-involved periampullary area, then followed with reconstruction. The pathologic specimen consisted of large polygonal cells with vesicular to fine chromatin nucleus, irregular nuclear membrane, and abundant eosinophilic cytoplasm. There were also extracellular keratin materials and presence of intercellular bridges between tumor cells. This morphology was compatible with squamous cell carcinoma. Therefore, the primary squamous cell carcinoma of distal CBD was diagnosed. Concurrent chemoradiation was administered for adjuvant therapy after post-operative recovery. The patient had been doing well for five months after surgery.

Keywords: Bile duct cancer, Cholangiocarcinoma, Squamous cell carcinoma, Adenocarcinoma, Choledochal cyst

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The malignancy of extrahepatic bile duct is common. It usually occurs in elderly patients and mostly was adenocarcinoma in histopathologic type. Interestingly, squamous cell carcinoma of biliary tract has been also reported in the literature. However, it is very rare, especially tumor located at extrahepatic bile duct. Since the first case of extrahepatic biliary squamous cell carcinoma was reported by Cabot in 1930, there had been less than 20 cases reported in the literature.

Case Report

A 36-year-old male patient without any underlying disease presented with obstructive jaundice for two weeks. He had also noticed dull aching pain at epigastrium and loss of appetite for a month before jaundice appeared. He had no fever or vomiting. At the first presentation, his liver function tests were total bilirubin 17.6 mg/dL, direct bilirubin 14.8 mg/dL, alkaline phosphatase 2,364 U/L, and albumin 1.9 g/dL, which were abnormal. Magnetic resonance cholangiopancreatography [MRCP] demonstrated dilated bilateral intrahepatic bile ducts with disproportional fusiform dilatation of extrahepatic bile duct about 7 cm in diameter and 12.3 cm in length as shown in Figure 1. The abrupt narrowing of the distal common bile duct [CBD] about 2.8 cm in length associated with enhancement of irregular periductal soft tissue was suggestive of a malignant feature. Therefore, the preoperative diagnosis was Choledochal cyst type 1 with suspicion of malignant distal CBD tumor. He was advised to improve his nutritional status and underwent percutaneous transhepatic biliary drainage [PTBD] with catheter inserted into right intrahepatic duct. Then, one week before the scheduled operation, he was admitted for oral and parenteral nutritional support. Pre-operative albumin rose up to 2.6 g/dL.

Intra-operatively, a 8×10 cm fusiform extrahepatic

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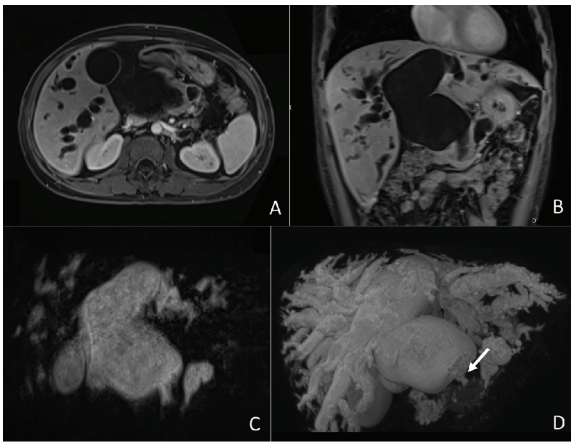

Figure 1. Axial view (A) and coronal view, (B) of MRI demonstrated large dilatation of extrahepatic bile duct with irregular periductal soft tissue thickening at distal CBD. MRCP (C, D) showed abrupt narrowing of distal CBD.

bile duct with surrounding dense adhesion was found. This finding made the dissection at hepatoduodenal ligament very difficult. After hepatic artery and portal vein were completely separated from the huge bile duct, the pancreaticoduodenectomy proceeded further. The bile duct was cut just below the confluence of the right and left hepatic duct. Then, the resection part of the pancreaticoduodenectomy was completed and the specimen was removed. The reconstruction was performed with Roux-en-Y fashion. Pancreaticojejunostomy and hepaticojejunostomy were anastomosed on the same jejunal limb, and then gastrojejunostomy was created on another limb. The operative time was about seven hours.

The pathologic specimen consisted of the distal part of stomach, duodenum, head of pancreas, extrahepatic portion of bile duct, and gallbladder. There was a well-demarcated, firm and non-homogeneous gray-white mass, size 5.5×4.5×3.5 cm, located at distal CBD and extended into the pancreatic parenchyma. The distal part of the stomach, duodenum, and gallbladder were unremarkable.

The microscopic features are illustrated in Figure 2. This lesion involved distal CBD and pancreas. It consisted of diffused sheets of mild to moderate differentiated tumor cells varying in size and irregular shape. They showed large polygonal cells with vesicular to fine chromatin nuclei, irregular nuclear membrane, and abundant eosinophilic cytoplasm. There were also extracellular keratin materials and presence of intercellular bridges between tumor cells. This histopathologic morphology was compatible with squamous cell carcinoma. The distal CBD also showed area of squamous metaplasia. Area of atypical glandular epithelial cells was not seen. R1 resection was determined because of microscopically detected posterior pancreatic margin involvement. No metastasis was found in 12 examined lymph nodes. The remaining gallbladder showed chronic cholecystitis without atypical cells. The duodenal mucosa was unremarkable.

Postoperatively, jejunostomy was used for early feeding while oral feeding continuously improved. Neither anastomotic leakage nor pancreatic fistula was evidenced during the postoperative care. However, superficial surgical site infection was detected on postoperative day 5 and was properly managed with drainage and wound dressing. PTBD was taken out on day 10 and then this patient was discharged on day 14. Despite thorough examination, the possible primary site of squamous cell carcinoma could not be identified.

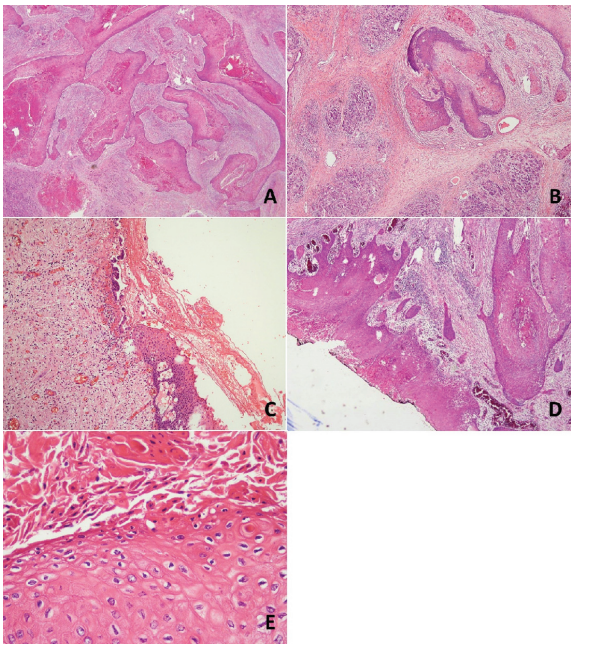

Figure 2. Microscopic examination demonstrated: A) on low-power (x40) microscopy, the large sheets of tumor cells with keratin materials in the center of sheets; B) on medium-power (x100) microscopy, the tumor invaded to pancreatic parenchyma; C) on medium-power (x100) microscopy, the junction between benign cuboid epithelial lining wall and squamous metaplasia at common bile duct; D) on low-power (x40) microscopy, areas of squamous cell carcinoma at common bile duct; E) on high-power (x400) microscopy, tumor cells with irregular nuclear membrane, vesicular to fine chromatin, eosinophilic cytoplasm, intercellular bridges and also keratin material.

Therefore, the primary squamous cell carcinoma of distal CBD was diagnosed. For adjuvant therapy, the patient underwent concurrent chemoradiation after post-operative recovery. The patient had been doing well for five months after surgery.

Discussion

According to worldwide data, most biliary malignant tumors are adenocarcinoma in histopathologic type. Other rare histologic variants include adenosquamous carcinoma, carcinosarcoma, neuro-endocrine tumors, metastatic tumors, and undifferentiated tumors[1,2]. The squamous cell carcinoma of biliary tract has also been reported in the literature. In 1930, the first case of squamous cell carcinoma of extrahepatic bile duct was reported by Cabot[1,3]. Since then, there had been less than 20 cases of pure squamous cell carcinoma of bile duct reported in the reviewed literature as shown in Table 1.

The pathogenesis of squamous cell carcinoma appearing on the columnar epithelium of the biliary mucosa was uncertain. The malignant transformation of squamous metaplasia induced by chronic inflammation on normal glandular epithelium was also proposed and it was supported by many cases that presented with identified cause of chronic inflammation. This theory was supported by finding of pure squamous cell carcinoma without adenocarcinoma component in biliary tumor[7]. The present case also demonstrated chronic inflammation from choledochal cyst with recurrent cholangitis. Although malignancy was universally known to be one of the consequences of choledochal cyst, most cases were adenocarcinoma. The choledochal cyst associated with squamous cell carcinoma had been previously mentioned by Stain et al[3] and Price et al[6]. Furthermore, Sewkani et al stated that the other probable etiology of squamous cell cancer was associated with ascariasis, liver fluke infestation, intrahepatic bile duct stone, Caroli's disease, choledocholithiasis, and primary sclerosing cholangitis[2]. However, some of the reported cases were not associated with any those causes. Lubana et al[1] and Yamana et al[7] mentioned the other possible mechanism, previously stated by Kohno et al, was the transformation of the adenocarcinoma to adenosquamous and eventually to squamous cell carcinoma, which frequently occurred in cases of gallbladder cancer. The interesting finding of an experimental animal model suggested adenosquamous carcinoma as transitional form of the histopathologic alteration from adenocarcinoma to squamous cell carcinoma[1,9].

The group of patients with squamous cell carcinoma of bile duct presented with the similar clinical setting to the patients suffering from adenocarcinoma, which was obstructive jaundice either with or without acute cholangitis. Blood for liver function and ultrasound were the initial diagnostic test. MRI with MRCP was the radiologic investigation of choice. ERCP was useful

Table 1. Previous case reports of squamous cell carcinoma of extrahepatic bile duct reviewed in the literature[7,8]

First author	Year	Age	Gender	Position	Operation	Chemotherapy	Radiation	Survival (months)
Cabot	1930	58	M	Proximal	Unknown	x	x	N/A
Burger	1978	24	F	Cystic duct junction	PD	o	x	8
Gulsrud	1979	68	M	Mid portion	Cholecystectomy with T-tube	x	x	6
Aranha	1980	58	F	Hilar	Cholecystectomy with T-tube	x	o	3
Clements	1990	73	M	Hilar	Biliary stent	x	x	N/A
Hirayasuyama	1990	68	M	Distal	PD	o	x	>3
Sakata	1991	68	M	Distal	PD	x	x	>27
Shibata	1994	50	M	Hilar	Extended left hepatic lobectomy	x	x	>10
Nakazaki	1996	75	M	Distal	PD	x	x	>6
Cho	2000	63	M	Distal	PD	x	x	N/A
Gatof et al.[4]	2004	86	F	Cystic duct junction	Cholecystectomy, biliary metallic stent	x	o	18
Sewkani et al.[2]	2005	60	M	Distal	PD	x	x	N/A
Abbas et al.[5]	2008	86	F	Hilar	Extended left hepatic lobectomy	x	o	>18
Price et al.[6]	2008	41	F	Hilar	Biliary stent	o	o	Unknown
Yamana et al.[7]	2011	66	M	Hilar	Extended right hepatic lobectomy	o	x	12
Goto et al.[8]	2016	77	F	Cystic duct junction	PD	o	x	32

M = male; F = female; PD = pancreaticoduodenectomy; N/A = not applicable

to relief biliary obstruction and to obtain brush cytology or biopsy of bile duct.

Pre-operative pathologic diagnosis of malignancy is usually difficult to obtain. Therefore, the decision of therapeutic management is similar to adenocarcinoma. Surgery is the treatment of choice with curative intention for resectable tumor. Evidence suggests that cholangiocarcinoma containing squamous cell carcinoma associated with the worse prognosis than adenocarcinoma histologic type because of more aggressive clinical behavior including vascular invasion, lymph node metastasis, and liver metastasis[1].

There is no well-established treatment guideline of chemotherapy or radiation therapy for squamous cell carcinoma of the biliary tract. Yamana et al treated liver metastasis detected six months after curative resection with first-line cisplatin and 5-fluorouracil and then second-line gemcitabine and S-1. Their patient survived for 12 months after the operation[7]. Goto et al administered eight courses of gemcitabine for adjuvant chemotherapy, however, local recurrence was detected at anastomosis of biliojejunostomy at 20 months[8]. Concerning radiation therapy, Abbas et al reported a female patient with squamous cell carcinoma of bile duct that underwent surgery with intraoperative radiotherapy of the resection field followed by postoperative external radiation. She survived more than 18 months without recurrence[5]. Catheter-delivered intraductal brachytherapy had been also used by Gatof et al for palliative treatment of their patient with 18-month survival[4].

Conclusion

Squamous cell carcinoma is an extremely rare malignancy of extrahepatic bile duct. One of possible etiologies is chronic inflammation associated with choledochal cyst. More studies regarding this rare tumor are needed for a better understanding in pathogenesis, prognosis, and optimal management. Surgical technique, endoscopic intervention, and guideline of adjuvant chemotherapy and radiotherapy should be further investigated to maximize the survival time and improve quality of life for this group of patients.

What is already known on this topic?

Malignancy of bile duct, so called cholangiocarcinoma, is a common malignant disease especially in Asia including Thailand. Almost all of them are adenocarcinoma in cell type. Surprisingly, squamous cell carcinoma was scarcely reported in the literature. There have been less than 20 cases of squamous cell carcinoma of extrahepatic bile duct reported for almost 90 years. Because of very low incidence, there has been inadequate information to describe natural history or prognosis, and to establish the proper management of this entity.

What this study adds?

This report described the clinical presentation, investigation, and management of a male patient with squamous cell carcinoma of extrahepatic bile duct. Interestingly, the malignant tumor of this patient was associated with choledochal cyst type 1. Although squamous cell carcinoma of extrahepatic bile duct was very rare as mentioned above, there were fewer cases of this type of tumor associated with choledochal cyst type 1 reported in the literature. This case report would provide more clinical, radiological, and pathological information of this rare tumor, and update information from the previously reported literature.

Potential conflicts of interest

The authors declare no conflict of interest.

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