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Signet Ring Cell Carcinoma of the Extrahepatic Bile Duct Diagnosed by Preoperative Biopsy: A Case Report

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Key Words

Bile duct carcinoma · Signet ring cell carcinoma · Jaundice

Abstract

A 73-year-old woman was admitted because of obstructive jaundice. Computed tomography revealed a stricture in the lower bile duct with enhanced bile duct wall. Endoscopic retrograde cholangiopancreatography (ERCP) revealed a tapering stenosis at the lower bile duct. Transpapillary histological biopsy using biopsy forceps through ERCP was performed; the diagnosis of signet ring cell carcinoma (SRCC) of the bile duct was established. Regional lymph node enlargement and distant metastases were not detected on diagnostic imaging. Pancreaticoduodenectomy with pylorus preservation was performed. Histological examination of the resected specimen confirmed SRCC of the extrahepatic bile duct coexisting with adenocarcinoma (ADC) of the extrahepatic bile duct with negative resection margins. However, tumor cells directly invaded the pancreatic parenchyma and the muscle layer of the duodenum, prompting us to administer adjuvant chemotherapy to the patient, with no sign of tumor recurrence at 1-year follow-up. Almost all tumors originating from the extrahepatic bile duct are ADC and other histological variants are rare. Of these, SRCC is extremely rare and only four cases have been reported. Furthermore, to the best of our knowledge, this is the first case report regarding the preoperative diagnosis of SRCC of the bile duct. Current reports indicate that younger age and Asian ethnicity are the clinical features of SRCC of the extrahepatic bile duct. Immunohistochemical staining of CK7, CK20 and MUC2 may be useful for predicting prognosis. Chemotherapy has not resulted in increased survival rates and only surgical resection currently serves as a curative treatment.

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Introduction

Carcinoma of the bile duct accounts for approximately 2% of all carcinomas and 0.5% of all carcinomas at autopsy [1, 2]. The peak incidence commonly occurs in the seventh decade of life, and patients are usually over 65 years of age [3]. Histopathologically, almost all tumors affecting the bile duct are well to moderately differentiated adenocarcinomas (ADCs), whereas other histological variants are less frequent; of these, signet ring cell carcinoma (SRCC) is extremely rare. This report presents the first case of SRCC of the extrahepatic bile duct that was successfully diagnosed by preoperative biopsy through endoscopic retrograde cholangiopancreatography (ERCP). The clinicopathological characteristics of the condition are also discussed.

Case Report

A 73-year-old woman was admitted to our hospital because of obstructive jaundice. Enhanced computed tomography revealed a hypervascular mass in the lower common bile duct and a stricture accompanied by a proximal dilatation of the bile duct (fig. 1). ERCP revealed stenosis at the lower bile duct. Transpapillary histological biopsy using forceps biopsy through ERCP was performed; a diagnosis of SRCC of the bile duct was then established (fig. 2). Regional lymph node enlargement and distant metastases were not detected on diagnostic imaging; thus, subsequent pancreaticoduodenectomy with pylorus preservation was performed. Histological examination of the resected specimen revealed a thickened wall with a whitish tumor with a size of 2.0 × 2.0 × 1.7 cm at the lower bile duct upon gross inspection.

Microscopically, the tumor was primarily composed of SRCC, partially coexisting with poorly differentiated ADC. Tumor cells contained mucin with vesicular nuclei and prominent nucleoli (fig. 3a), infiltrating the pancreatic parenchyma and involving the muscularis propria of the duodenum. None of the lymph nodes presented metastases. Immunohistochemical staining showed tumor cells that were positive for CK7 (fig. 3b), but negative for both CK20 (fig. 3c) and MUC2 (fig. 3d). Finally, the tumor was diagnosed as T3N0M0 stage III according to the International Union Against Cancer TNM classification, and the patient received adjuvant chemotherapy using cisplatin + gemcitabine without signs of tumor recurrence at 1-year follow-up.

Discussion

SRCC commonly occurs in the gastrointestinal tract, particularly in the stomach, and sometimes occurs in the gallbladder or ampulla. However, SRCC of the biliary tract is extremely rare, and the clinicopathological characteristics are unclear. Previously, only four cases of primary SRCC of the extrahepatic bile duct have been reported in the literature. Most of the reports were from Asian countries (4 out of 5 patients), and from these reports and the present case, 60% were male. The mean age was 61.5 years (range 42–78 years), which was younger than that observed in common biliary tract cancer. Jaundice was the most common symptom (4 out of 5 patients).

Since SRCC progresses rapidly, it often results in poor prognosis. Among the previous four cases of biliary SRCC, two underwent surgical intervention (one patient underwent surgery and the other had surgery with adjuvant chemoradiation), and no signs of recur-

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rence were reported (table 1). The two patients who had unresectable advanced cancer died within 3 months (one received chemotherapy and the other was under observation). Only surgical resection has been suggested as a curative treatment, and neither chemotherapy nor radiotherapy appeared to show survival benefits in these patients.

The histological origin of SRCC in the extrahepatic bile duct remains elusive. To date, two theories involving the periampullary area have been proposed; one states that SRCC develops on the ectopic gastric mucosa [4, 5], and the other states that the gastric-type metaplastic change of duodenal epithelium may be the origin of SRCC [5–7]. However, the present case showed neither ectopic gastric mucosa nor metaplastic changes in the surgical specimen. One more possible origin of SRCC is from ADC that marginally coexists in the transitional zone. We speculate that SRCC in this case had dedifferentiated from the pre-existing ADC.

Roh et al. [8] demonstrated the association between immunohistochemical markers and the prognosis of SRCC of the extrahepatic bile duct. Carcinoma immunoprofiling has identified the intestinal and the pancreatobiliary type of SRCC. The intestinal type is negative for CK7, but positive for CK20/MUC2, which is strongly associated with better prognosis. On the other hand, the pancreatobiliary type is positive for CK7 but negative for CK20/MUC2 and has been associated with poorer prognosis [9]. The present case was positive for CK7, but negative for CK20/MUC2; therefore, the case was considered to be the pancreatobiliary type and was expected to have a poor prognosis. Although the patient had no evidence of recurrence at 1-year follow-up, the clinical course had to be closely monitored.

Pathological diagnosis of a malignant lesion is vital to the decision-making process of whether surgical resection or chemotherapy is the appropriate treatment. A pathological diagnosis is usually established after bile cytology, biliary brushing cytology or biliary biopsy. Previous studies have shown that the sensitivity of biliary biopsy is higher than other transpapillary sampling methods. This is the first case of SRCC in whom an accurate preoperative diagnosis could be made by using transpapillary bile duct biopsy. Although the immunochemical profile of this case suggested a poorer prognosis, correct preoperative diagnosis was helpful in the subsequent early-stage surgical resection and in improving the patient's prognosis. The clinicopathological features and prognosis of biliary SRCC remain unclear due to its rarity; therefore, more extensive investigations are warranted.

Disclosure Statement

The authors have no potential conflicts of interest.

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Table 1. Reported cases of SRCC of the extrahepatic bile duct

Case study	Age, years	Sex	TNM stage	Treatment	Histo-pathology	Outcome
Hiraki et al., 2007 [10]	78	m	–	chemotherapy	SRCC	3 months
Ogata et al., 2010 [11]	42	f	T4N1M0	PD	SRCC + ADC	alive
Lee et al., 2010 [12]	55	m	T3N1M0	PD + CRT	SRCC	alive
Matsumoto et al., 2011 [13]	72	m	T4N3M1	none	SRCC	3 months
Present study	73	f	T3N0M0	PD	SRCC + ADC	alive

CRT = Chemoradiation therapy; PD = pancreaticoduodenectomy.



Fig. 1. Enhanced computed tomography demonstrating a hypervascular mass in the lower common bile duct.

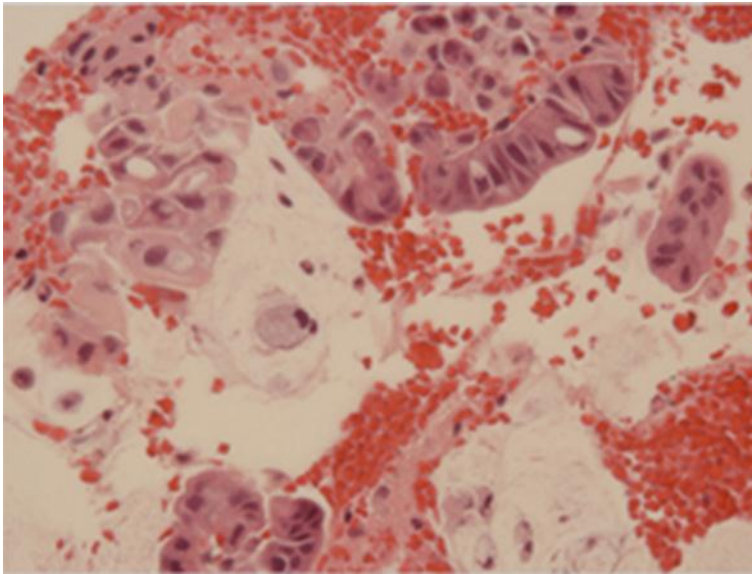


Fig. 2. The biopsy specimen contained abundant intracytoplasmic mucin and nuclei (H&E staining, ×400).

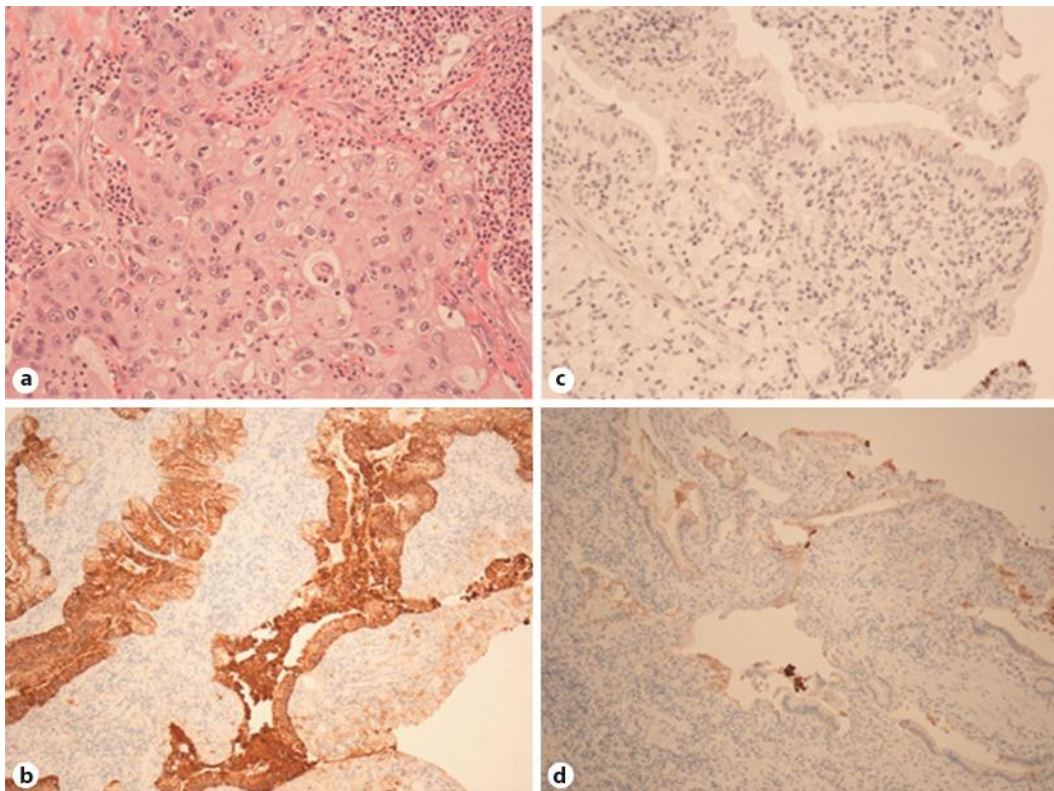


Fig. 3. **a** The tumor was histopathologically composed of SRCC and poorly differentiated ADC (H&E staining, ×400). **b–d** Immunohistochemical findings for CK7 (**b**, ×100), CK20 (**c**, ×100) and MUC2 (**d**, ×100).