Scholars Journal of Medical Case Reports **ISSN 2347-6559 (Online)**
Sch J Med Case Rep 2016; 4(12):902-905 **ISSN 2347-9507 (Print)**

(An International Publisher for Academic and Scientific Resources) DOI: 10.36347/sjmcr.2016.v04i12.007

Adenosquamous Carcinoma of Lower Extrahepatic Biliary Tract: A case report

Takashi Yamada[1], Nobuhiro Takeuchi[2*], Yusuke Nomura[1], Masanori Takada[1], Akihito Otsuka[1]
[1]Department of Internal Medicine, Kawasaki Hospital, Japan
[2]Department of Internal Medicine, Kobe Tokushukai Hospital, Japan

***Corresponding author**
Nobuhiro Takeuchi
Email: nobuhiro.takeuchi@tokushukai.jp

Abstract: Adenosquamous carcinoma, consisting of adenocarcinoma and squamous cell carcinoma, rarely occurs in the extrahepatic bile duct. Due to nonspecific imaging findings, preoperative diagnosis of adenosquamous carcinoma depends exclusively on brushing cytology or biopsy performed under endoscopic retrograde cholangiopancreatography (ERCP). However, correct diagnosis before surgical resection is challenging in some patients. Here, we report the case of a patient with adenosquamous carcinoma in the lower extrahepatic bile tract diagnosed using brushing cytology under ERCP.
Keywords: Adenosquamous carcinoma, squamous cell carcinoma, endoscopic retrograde cholangiopancreatography (ERCP).

INTRODUCTION

Adenosquamous carcinoma is characterized by the histological presence of both adenocarcinoma and squamous cell carcinoma within the same tumor. Compared to adenocarcinoma, adenosquamous carcinoma has a lower incidence and poor prognosis. A histological study reported that adenosquamous carcinoma of the extrahepatic biliary tract comprised only 4.7% of all cancers occurring in the extrahepatic biliary tract [1]. Clinical and histological features of adenosquamous carcinoma remain largely unknown, and a definitive diagnosis before surgical resection is challenging. Here, we report the case of a patient with adenosquamous carcinoma of the lower extrahepatic biliary tract.

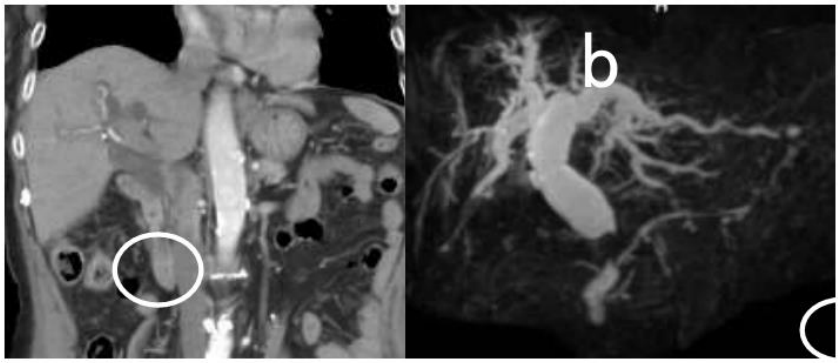
CASE PRESENTATION

An 82-year-old female with a history of laparoscopic cholecystectomy visited our hospital for further examination of abnormal hepatic and biliary enzyme levels. Her past history included hypertension and diabetes mellitus, both of which were treated with medication.

Blood chemistry analysis revealed mildly elevated liver and biliary enzymes; the results are as follows: total bilirubin, 2.3 mg/dl; direct bilirubin, 1.5 mg/dl; gamma-glutamyl transpeptidase, 1473 IU/ml; alkaline phosphatase, 1143 IU/ml; aspartate aminotransferase, 332 IU/L; and alanine aminotransferase, 137 IU/L. Her carcinoembryonic antigen (CEA) level was within normal limits at 4.1 ng/ml, but cancer antigen 19-9 (CA19-9) was moderately elevated at 196.7 U/ml. SCC and CYFRA, two tumor markers, were slightly increased at 1.9 ng/ml and 4.0 ng/ml, respectively.

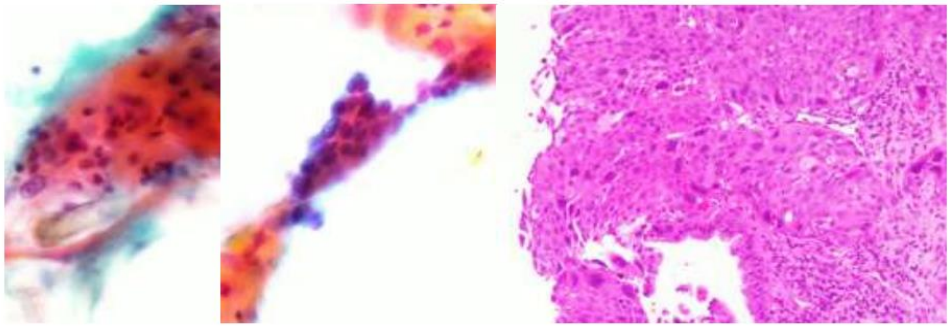
Contrast enhanced computed tomography (CT) and magnetic resonance cholangiopancreatography (MRCP) revealed marked dilatation of the intrahepatic bile duct and upper and middle extrahepatic bile duct, with narrowing of the lower extrahepatic bile duct (Figure 1). Bulky mass was not apparent in any of the images. Brushing cytology under endoscopic retrograde cholangiopancreatography (ERCP) revealed squamous cell carcinoma (Figure 2a, left), with suspicious adenocarcinoma (Figure 2a, right). Biopsy specimens obtained during ERCP revealed squamous cell carcinoma (Figure 2b). These findings led to the preoperative diagnosis of squamous cell carcinoma in the lower extrahepatic bile duct. Surgery performed in this patient revealed a mass in the lower extrahepatic duct (Figure 3a), with a slight invasion into pancreas, and no hepatic metastasis, peritoneal dissemination, or ascites; thus, subtotal stomach-preserving pancreaticoduodenectomy (SSPPD) was performed. Microscopic surgical specimens stained with hematoxylin–eosin (Figure 3b, low-power field; and Figure 3c, high-power field) revealed alveolar proliferation of atypical cells with clear and eosinophilic cytoplasm, suggesting squamous cell carcinoma, and annular and cribriform proliferation of atypical cells with mucus, suggesting adenocarcinoma. Pathological assessment revealed papillary-infiltrating type of adenosquamous carcinoma, with vascular and lymphatic invasion. Immunohistochemical staining determined that cancer cells were positive for cytokeratin 5/6 (Figure 3d), PAS-A1B (Figure 3e), and p63 (Figure 3f), leading to a definitive diagnosis of

adenosquamous carcinoma of the extrahepatic bile duct in this patient. Postoperative pathological evaluation determined that the cancer was T3N1M0, stage IIB.



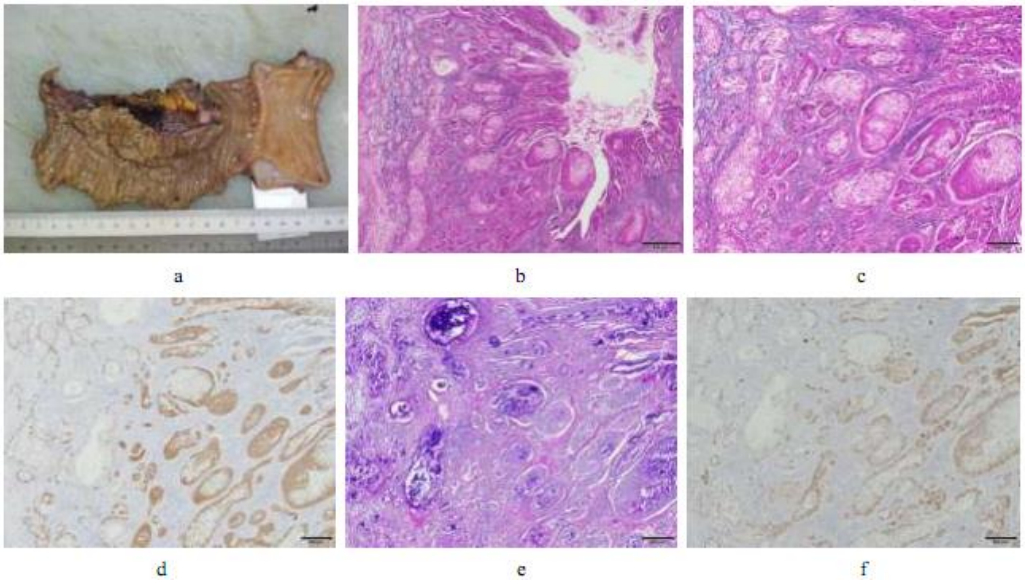
a b

Fig-1: Contrast enhanced computed tomography (a) and Magnetic Resonance Cholangiopancreatography (b) reveal marked dilatation in the intrahepatic bile duct and upper and middle extrahepatic bile duct, with a narrowed lower extrahepatic bile duct



a b

Fig-2: Brushing cytology under Endoscopic Retrograde Cholangiopancreatography (ERCP) revealed squamous cell carcinoma (a; left), with suspicion of adenocarcinoma (a; right) by brushing cytology. Biopsies under ERCP revealed squamous cell carcinoma (b)



a b c

d e f

Fig-3: a: operative specimen, b and c: microscopic specimen reveals adenocarcinoma (circle) and squamous (square) carcinoma components (hematoxylin and eosin, b:low-power field, c:high-power field), immunostaining of cancer cells by cytokeratin 5/6 (d), PAS-A1B (e), and p63 (f) is positive

The postoperative course was uneventful, and no recurrence was detected without chemotherapy at 14 months after the operation.

DISCUSSION

Adenosquamous carcinoma is defined by the presence of both adenomatous and squamous components, in which the latter comprises over a fourth of the tumor. The incidence of adenosquamous carcinoma in the gastrointestinal system is 0.74% [1]. It is detected more frequently in the biliary system (2.65%) (gallbladder, 5.23%; bile duct, 1.28%) than in the stomach (0.54%) and colon (0.27%) [1]. Mucous membranes in the bile duct and gallbladder have no squamous epithelium, and squamous cell carcinoma is hypothesized to originate from glandular tissues. There are four proposed mechanisms for the development of adenosquamous carcinoma: i) ectopic squamous epithelium, ii) squamous metaplasia of biliary epithelium, iii) squamous metaplasia of glandular system, and iv) histological transformation of adenocarcinoma. Up to date, evidence from several studies suggest that histological transformation of adenocarcinoma to squamous cell carcinoma might be the underlying mechanism [2-4].

Okabayashi *et al*. [5], who reviewed 36 Japanese cases of adenosquamous carcinoma of the extrahepatic bile duct between 1975 and 2003, reported that it occurred slightly more frequently in males than in females at a ratio of 7:5 and that the average age was 60.5 years. Initial manifestations included abdominal pain, jaundice, general fatigue, and weight loss. In that study, chemical analysis revealed elevated total bilirubin, CEA, and CA19-9 in 92.6%, 52.4%, and 77.3% of the patients, respectively. It is nearly impossible to differentiate adenocarcinoma from adenosquamous carcinoma based on only clinical symptoms and laboratory data. At the time of diagnosis, 37% of cases are at an early stage of I and II. In contrast, 33.3% present with end stage disease, stage IV. Its prognosis is poor; average survival is 13 months, and the overall five-year survival is 16%.

A study Kim *et al*. [6] investigating CT findings in patients with primary adenosquamous carcinoma of the extrahepatic bile duct concluded that differentiating adenosquamous carcinoma from adenocarcinoma was almost impossible by CT alone. Symptoms of carcinoma of the extrahepatic bile duct are present in early stage disease due to the characteristics of the bile duct, whereas detection of a tumor developing along the lumen before it grows into a bulky mass is difficult via initial CT findings. Similarly, it was not possible to suspect adenosquamous carcinoma with imaging modalities alone in our case.

Generally, adenosquamous carcinoma has a poor prognosis compared to cancers with other histological origins within the bile duct due to its tendency to aggressively invade lymph nodes, vessels, nerve plexuses, and pancreas [7]. In addition, squamous component of this type of tumor was reported to proliferate two times faster than its adenomatous component [8]. The compression of adenomatous components by squamous proliferation leads to the loss of a distinct border between the two components. Furthermore, with tumor progression, squamous cell proliferation continues to replace adenocarcinoma. Tumors with a higher percentage of squamous components tend to progress more rapidly and have poorer prognosis.

The preoperative diagnosis of adenosquamous carcinoma of the extrahepatic bile duct by brushing cytology is difficult. Sakurai *et al*. reported that the detection rates of squamous or adenosquamous components by brushing cytology were as low as 26.7% [9]. Repeated cytology in combination with biopsy may be required for proper preoperative histological diagnosis. There are no specific findings by ERCP, CT, or MRI; therefore, cytology along with biopsy during endoscopy may provide an improved approach for successful preoperative diagnosis.

CONCLUSION

We herein reported a patient with adenosquamous carcinoma of the lower extrahepatic biliary tract. While imaging modalities could not differentiate between adenosquamous carcinoma and adenocarcinoma of the bile duct, preoperative diagnosis by biopsy suggested squamous carcinoma with a suspicion of adenosquamous carcinoma. Preoperative diagnosis of adenosquamous carcinoma of the bile duct remains challenging due to the absence of overt characteristic features associated with adenosquamous carcinoma by imaging modalities. However, meticulous examination of cytology and biopsy during endoscopy may aid in proper preoperative diagnosis.

REFERENCES

1. Kiuchi S, Koike S, Takashi Ha, Nagamine M, Nishida K. Three Cases Of Adenosquamous Carcinoma Of The Extrahepatic Bile Tract. The journal of the Japanese Practical Surgeon Society. 1988 Feb 25;49(2):350-6.
2. Cao SH. Extrahepatic bile duct cancer. Report of 106 cases. Chinese medical journal. 1992 Aug;105(8):622-9.
3. Iemura A, Yano H, Mizoguchi A, Kojiro M. A cholangiocellular carcinoma nude mouse strain showing histologic alteration from adenocarcinoma to squamous cell carcinoma. Cancer. 1992;70(2):415-422.
4. Momosaki S, Yano H, Kojiro M. Establishment of a human hepatic adenosquamous carcinoma cell line (KMC-2) and its response to cytokines. Pathol Int. 1995;45(2):137-146.
5. Okabayashi T, Kobayashi M, Nishimori I, Namikawa T, Okamoto K, Onishi S, Araki K.

Adenosquamous carcinoma of the extrahepatic biliary tract: clinicopathological analysis of Japanese cases of this uncommon disease. Journal of gastroenterology. 2005 Feb 1;40(2):192-9.

6. Kim KW, Kim SH, Kim MA, Lee JM, Park HS, Kim JY, Lee JY, Han JK, Choi BI. Adenosquamous carcinoma of the extrahepatic bile duct: clinicopathologic and radiologic features. Abdominal imaging. 2009 Apr 1;34(2):217-24.
7. Hong SM, Kim MJ, Jang KT, Yoon GS, Cho H, Frierson HF, Yu E. Adenosquamous carcinoma of extrahepatic bile duct: clinicopathologic study of 12 cases. Int J Clin Exp Pathol. 2008 Jan 1;1(2):147-56.
8. Charbit A, Malaise EP, Tubiana M. Relation between the pathological nature and the growth rate of human tumors. Eur J Cancer. 1971;7(4):307-315.
9. Sakurai Y, Nakazawa K, Yamashita T, Tokura K, Asada K, Takebayashi J. A Case Of Adenosquamous-Cell Carcinoma Of The Lower Bile Duct Diagnosed By Cytology Of The Bile. Nihon Rinsho Geka Gakkai Zasshi (Journal Of Japan Surgical Association). 2000 Sep 25;61(9):2458-62.