

## Case Report

# Primary adenosquamous carcinoma of the liver: a case report and review of the literature

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**Abstract:** Primary adenosquamous carcinoma of the liver is a rare subtype of cholangiocarcinoma. Adenosquamous carcinoma, which consists of both adenocarcinoma and squamous cell carcinoma components. A 73-year-old woman was admitted to our hospital with a 1-year history of anorexia and general fatigue. Abdominal computed tomography (CT) disclosed a mass, 8 cm in diameter, with low-density located and central necrosis in the right lobe segment of the liver. Because of the rapid development of the liver tumor, the patient died of liver failure 10 months after the surgery.

**Keywords:** Primary liver tumor, adenosquamous carcinoma

## Introduction

Most malignant primary tumors of the liver are hepatocellular carcinoma and cholangiocarcinoma. Primary adenosquamous carcinoma (ASC) of the liver is a rare subtype of cholangiocarcinoma. Adenosquamous carcinoma, which consists of both adenocarcinoma and squamous cell carcinoma components, is extremely rare. ASC tends to present more aggressive clinicopathologic features and has a worse prognosis than cholangiocarcinoma [1, 2]. In this study, we present a rare case of primary ASC and review of the literature. At laparotomy, an extended right lobectomy and an excision of the involved gallbladder were done. Microscopically, the tumor contained definite components of both adenocarcinoma and squamous cell carcinoma.

## Case report

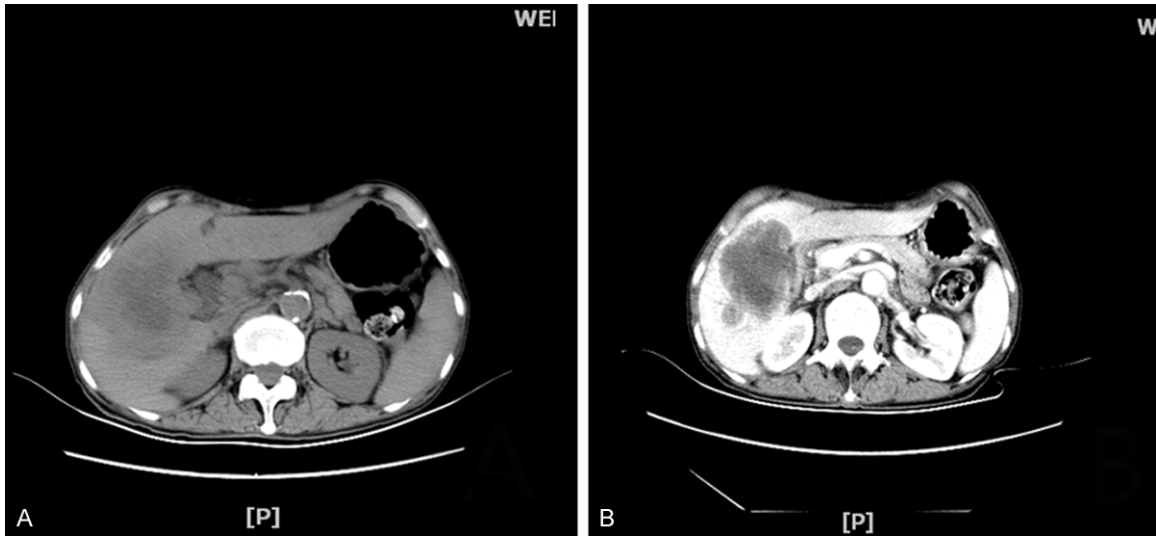
A 73-year-old woman was admitted to our hospital for a general fatigue, anorexia, on July 4, 2014. She had a surgical history of hysterectomy due to uterine fibroids. On physical examination, her body temperature was 37.5 degrees. Superficial lymph nodes were not palpable. There was not any jaundice and ascites.

Abdominal examination revealed a tender liver, extending one fingerbreadths below the right costal margin.

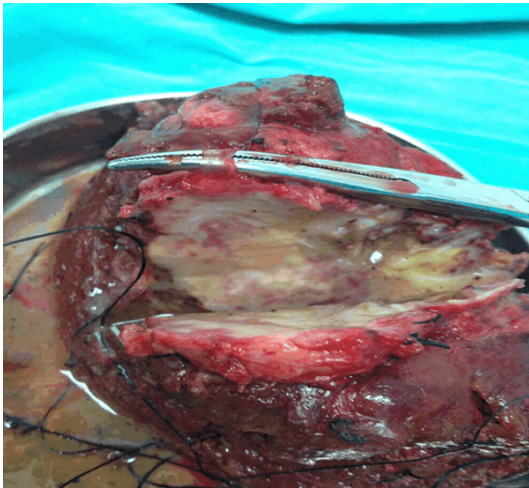
The results of relevant laboratory studies were: WBC 16,000/mm<sup>3</sup>, RBC 359×10<sup>4</sup>/mm<sup>3</sup>, Hb 10.2 g/dL, platelet 148,000/mm<sup>3</sup>, aspartate aminotransferase 15 U/L, alkaline phosphatase 27 U/L, total bilirubin 0.4 mg/dL, total protein 6.4 g/dL, α-fetoprotein (AFP) 1.9 ng/ml (normal range, <9 ng/ml), carcinoembryonic antigen (CEA) 6.9 ng/ml (normal range, <5 ng/ml), carbohydrate antigen (CA) 199, 200 U/ml (normal range, <35 U/ml). HBsAg and anti-HCV antibody were both negative.

Abdominal computed tomography (CT) disclosed a mass, 8 cm in diameter, with low-density located and central necrosis in the right lobe segment of the liver. The enhanced abdominal CT showed a peripheral irregular rim enhanced mass in the left lobe of the liver without lymph node enlargement (**Figure 1**).

At laparotomy, the tumor occupied the right lobe of the liver and invaded the gallbladder. Mass sticks with transverse colon. There was no lymphadenopathy in the adjacent area. There were no metastatic lesions in the lateral



**Figure 1.** A. Abdominal computed tomography (CT) disclosed a mass, 8 cm in diameter, with low-density located and central necrosis in the right lobe segment of the liver. B. The enhanced abdominal CT showed a peripheral irregular rim enhanced mass in the left lobe of the liver without lymph node enlargement.



**Figure 2.** The cut surface of the resected specimen showed a yellowish white solid tumor, measuring 8×7×7 cm, with peripheral necrosis.

segment of the liver or distant organs. An extended right lobectomy and an excision of the involved gallbladder were done. The cut surface of the resection specimen showed a yellowish white solid tumor, measuring 8×7×7 cm, with peripheral necrosis (**Figure 2**). Microscopically, the tumor contained definite components of both adenocarcinoma and squamous cell carcinoma. The tumor consisted predominantly of well differentiated squamous cell carcinoma with keratinization, intercellular bridged (**Figure 3A**). A transition area between adeno-

carcinoma and squamous cell carcinoma was recognized (**Figure 3B and 3C**). There were no metastases in the dissected lymph nodes. Take into account these findings; this tumor was diagnosed as ASC of the liver.

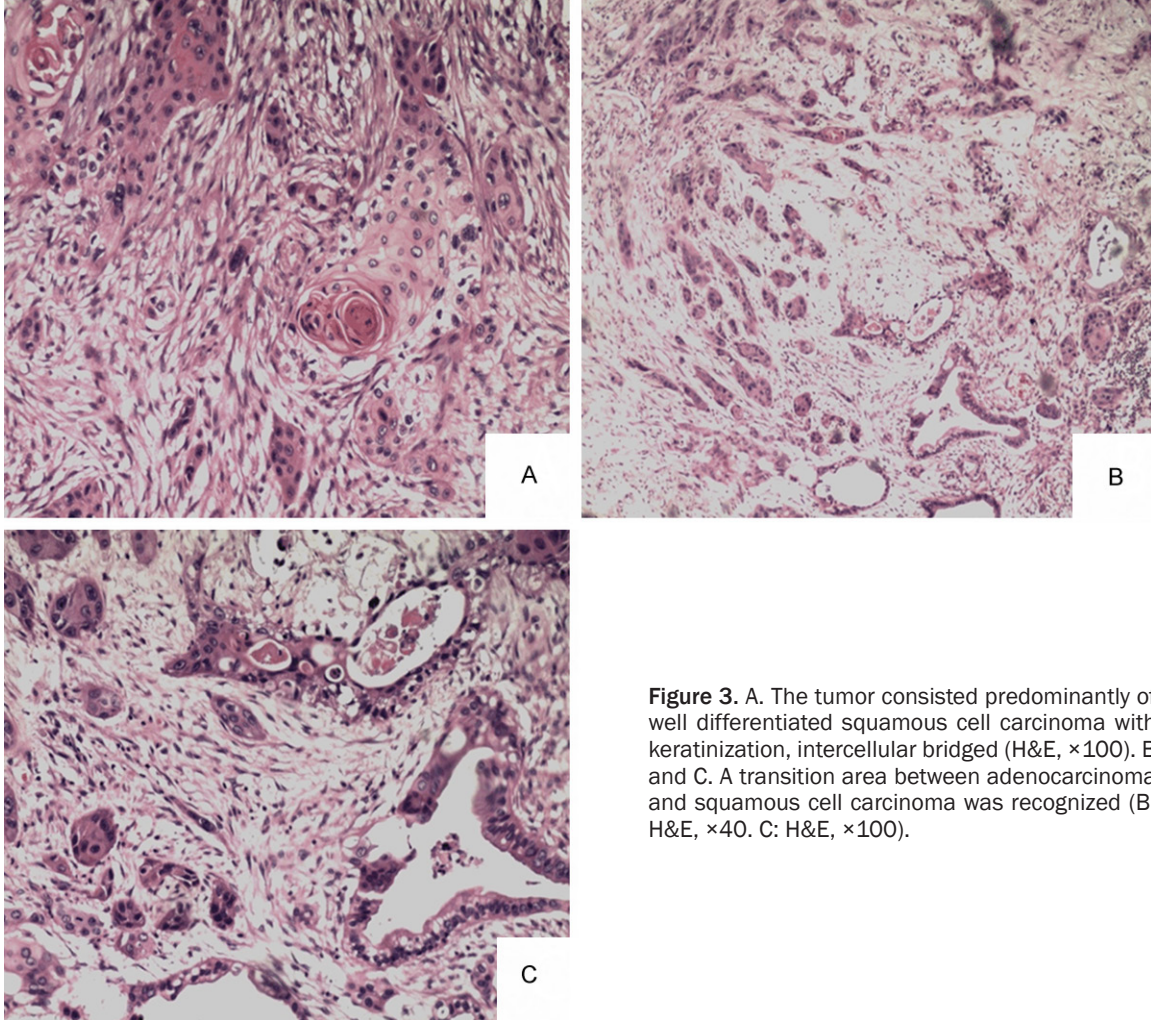
The postoperative course was uneventful. Three months after the operation, serum AFP and CA199 returned to normal levels (1.9 ng/ml and 19.9 U/ml). However, five months after the operation, serum CA125 and CA199 turned to high levels (111.7 U/ml and 96.4 U/ml). Because of the rapid development of the liver tumor, the patient died of liver failure 10 months after the surgery.

#### Discussion

ASC sometimes develops in the stomach, pancreas, gallbladder and thyroid, but rarely in the liver [3, 4]. Only 59 cases have been reported since Pianzola and Durt [5] first described it in 1971. Carcinomas containing both adenocarcinoma and squamous cell carcinoma components have been referred to as ASC [6], adenoacanthoma and mucoepidermoid carcinoma [5].

ASC consists of both adenocarcinoma and squamous cell carcinoma components. Squamous differentiation is evident by individual cell keratinization, intercellular bridges, keratin pearl formation and/or dyskeratosis and glan-

## Liver adenosquamous carcinoma



**Figure 3.** A. The tumor consisted predominantly of well differentiated squamous cell carcinoma with keratinization, intercellular bridged (H&E,  $\times 100$ ). B and C. A transition area between adenocarcinoma and squamous cell carcinoma was recognized (B: H&E,  $\times 40$ . C: H&E,  $\times 100$ ).

dular differentiation by various-sized gland formations and intracellular and intraluminal mucin.

The preoperative diagnosis was extremely difficult. The majority of ASC cases in the liver are detected at an advanced stage. Most patients have a large mass and extensive invasion into the perihepatic region and lymphatics. As shown in **Table 1**, they were between 35 and 77 years of age (mean 59.8 years). The initial symptoms were abdominal pain, general fatigue, fever, anorexia and jaundice. The tumor was located in the left hepatic lobe in 12 patients (60%), the right hepatic lobe in 8 (40%). 21 patients underwent surgery, including the present patient. The main treatment of choice for this tumor is hepatectomy: left lobectomy in 9 patients, right lobectomy in 5, right trisegmentectomy in 2, tumor resection in 1, and choledochotomy in 1, left hemihepatectomy

in 1, right hepatectomy in 1. Twelve Of the 20 patients died of widespread metastases within 1 year. The 1-year survival rate was 45%. Survival of patients was between 1 and 96 months, and their mean survival was 13.6 months. Uenishi et al [7] reported the 1-year survival rates for intrahepatic cholangiocarcinoma were 68%. The prognosis of patients with primary ASC of the liver seems to be poorer than that of patients with the common type of cholangiocellular carcinoma of the liver. Takahashi et al [2] use the nuclear DNA analysis technology. His finding suggested that the more malignant biological behavior of the SCC component was responsible for the rapid growth and the aggressive clinical course of the tumor. Kobayashi et al [8] revealed that lymph node metastasis and the elevation of total bilirubin were associated with poor survival after surgery, and lymph node metastasis, intrahepatic metastasis, location of tumor in



## Liver adenosquamous carcinoma

**Table 1.** Operative cases of ASC, AA, and MEC of the liver

Case	Author	Age	Symptoms	Site	Preoperative diagnosis	Operation	Size (cm)	Pathological diagnosis	Outcome
1	Pianzola [5]	44	Fever	R	Hydatid cyst	Rt. lobectomy	15×10×10	MEC	45 D Died
2	Koo [12]	44	Fever, epigastralgia	L	CCC	Lt. lobectomy	12	MEC	6 M Died
3	Moore [13]	64	Fever	R	Hepatic abscess	Rt. hepatectomy	10×9×9	ASC	4 M Died
4	Tomioka [1]	59	Jaundice	L	CCC	Lt. lobectomy	4.4×2.8	ASC	17 M Died
5	Hayashi [14]	40	Rt. hypochondralgia	L	ND	Tumor resection	3×3×2	MEC	8 M Died
6	Hu [15]	40	Epigastralgia, anorexia	L	Hepatolithiasis	T-Tube choledochotomy	15	ASC	1 M Died
7	Hu [15]	46	Epigastralgia	L	Hepatolithiasis	Lt. lobectomy	11×9.5×7.5	ASC	17 M Died
8	Suga [16]	74	Jaundice	R	CCC	Rt. lobectomy	2.2×1.5×2	ASC	8 M Died
9	Suga [16]	58	Epigastralgia	L	CCC	Lt. lobectomy	6×5×5	ASC	18 M Died
10	Hamaya [10]	72	Epigastric mass	L	CCC	Lt. lobectomy	15×13.5×9	ASC	16 W Died
11	Higuchi [17]	72	General fatigue, weight loss	L	CCC	Lt. lobectomy	11×10×10	ASC	2 M Died
12	Yamamoto [18]	69	General fatigue, fever	R	CCC	Rt. trisegmentectomy	6×6	ASC	8 M Died
13	Ochiai [19]	77	Fever, abdominal pain	L	CCC	Lt. lobectomy	1×0.9×0.7	ASC	27 M Died
14	Takahashi [2]	68	Fever, jaundice	R	CCC	Rt. trisegmentectomy	6×5.5×4	ASC	3 M Died
15	Kwon [20]	63	Fever	L	Adenocarcinoma	Lt. lobectomy	6×5×5	ASC	8 M Alive
16	Suzuki [21]	67	Fever	L	CCC	Lt. lobectomy	8×7×6	ASC	14 M Died
17	Kobayashi [8]	54	liver dysfunction	R	ND	Rt. lobectomy	5×4.2×3.5	ASC	17 M Died
18	Demir [22]	35	Epigastralgia	R	Squamous cell carcinoma	Rt. lobectomy	5×5	ASC	8 Y Alive
19	Shimizu [23]	76	Epigastralgia	L	CCC	Lt. hemihepatectomy	4.5×4	ASC	3 M Alive
20	Present case	73	Anorexia, general fatigue	R	Liver tumor	Rt. lobectomy	8×7×7	ASC	10 M Died

ASC, Adenosquamous carcinoma; AA, adenoacanthoma; MEC, mucoepidermoid carcinoma; CCC, cholangiocellular carcinoma; Rt., right; Lt., left; Abd., abdominal; R, right; L, left; D, days; W, weeks; M, months; Y, years.

## Liver adenosquamous carcinoma

the right lobe, and the pathologic stage were significant factors for all cases.

The pathogenesis of ASC in the liver remains unknown, with two major hypotheses in existence. Continuous irritations of the bile duct and various congenital cysts of the biliary tract by chronic inflammation or infection can induce metaplastic changes in the biliary epithelium and have been thought to lead to neoplasia [9]. Barr and Hancock [6], Hamaya et al [10], and others [2, 11] have suggested that the ASC arose from squamous metaplasia of adenocarcinoma cells. Because there was no normal epithelium in the tumors they observed, and the tumors contained only adenocarcinoma, adenocarcinoma metaplasia, and squamous cell carcinoma components.

The treatment of choice for this tumor is hepatectomy. Some report advocated radiation therapy, because squamous carcinoma is more sensitive to radiation therapy than adenocarcinoma [1]. Postoperative adjuvant therapy such as chemotherapy and/or radiotherapy should be started as soon as possible. In our case, the patient was treated with an extended right lobectomy and involved gallbladder. Our patient did not receive adjuvant therapy. The patient died of liver failure 10 months after the surgery.

### Disclosure of conflict of interest

None.

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## Liver adenosquamous carcinoma

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