Primary squamous cell carcinoma of the liver with immunohistochemical evidence

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This paper reports a case of primary squamous cell carcinoma (SCC) of the liver. The patient had a large mass between the left lateral segment of the liver and the lesser curvature of the stomach on computed tomography. Ultrasonography-guided fine needle aspiration of the mass was suggestive of a well-differentiated SCC. A left lobectomy of the liver and wedge resection of the stomach were performed. The pathology showed positive immunoreactivity for cytokeratin 19 (CK19), carcinoma-embryonic antigen and high-molecular-weight cytokeratin, and negative immunoreactivity for CK8, CK18 and hepatic-specific antigen. (Korean J Med 77:113-117, 2009)

Key Words: Liver tumor; Squamous carcinoma; Immunohistochemistry

INTRODUCTION

Primary squamous cell carcinoma (SCC) of the liver is extremely rare. It may not originate directly from the liver tissue, but from the lining of a developmental hepatic cyst\(^{1,2}\), a hepatic teratoma, or hepatolithiasis\(^{3,4}\). Here, we report a patient in whom primary SCC originated from hepatocytes directly.

CASE REPORT

A 42-year-old woman was admitted with epigastric pain. She suffered from early satiety and general fatigue for 3 months. She had not been exposed to hepatitis virus or potentially hepatotoxic drugs. She did not drink alcoholic beverages. On admission, her temperature was 36.5°C and the liver was not palpable below the costal margin. Laboratory studies showed the following: hematocrit 31.9%, white cell count...
Abdominal ultrasonography showed a large mass of heterogeneous echogenicity between the left lobe of the liver and stomach. Computed tomography (CT; Fig. 1) showed an 8-cm low-attenuated mass with peripheral enhancement in the left lateral segment of the liver, adhering to the stomach. The gastric wall adjacent to the mass was thickened and the mass was compressing the left lobe of the liver. No lymph node enlargement was found.

Esophagogastroduodenoscopy revealed no definite abnormality except mild gastritis. Endoscopic ultrasonography (EUS) (Fig. 2) showed a large heterogenous mass outside the serosa of the stomach, and the border between the mass and serosa was indistinct.

Ultrasonography-guided fine needle aspiration of the mass suggested a well-differentiated SCC. At laparotomy, a large tumor was apparent in the left lobe of the liver and it was adherent to the lesser curvature of the stomach. She underwent a left lobectomy of the liver and wedge resection of the stomach.

The resected liver measured 10×9×6 cm (Fig. 3). On serial
Figure 4. The liver mass contained well-differentiated squamous cells, with (A) intracellular keratin production (hematoxylin and eosin stain, ×200 magnification) and positive immunoreactivity for (B) CEA and (C) HMW CK (×150 magnification).

DISCUSSION

In this case, the physical examination and investigations failed to reveal another primary site for the SCC of the liver, even in the usual primary sites for SCC; the investigations included an endoscopic examination of the gastrointestinal tract, and radiological imaging of the chest and abdomen, including abdominal ultrasound and CT. Therefore, the tumor could be a primary SCC of the liver.

In the liver, the epithelial cells of both hepatocytes and bile duct cells express cytokeratin (CK). This expression pattern is believed to be preserved during neoplastic transformation. Therefore, an evaluation of the CKs in the liver is considered useful for establishing the cellular origin of a neoplasm.
Normal human hepatocytes and hepatocellular carcinoma express CK8 and CK18, whereas bile duct cells and carcinomas contain CK7 and CK9 in addition to CK8 and CK18. Previous studies observed that SCC was uniformly positive for HMW CK, whereas adenocarcinoma (AC) was negative\(^7,8\).

Authors have reported at least five processes for the histogenesis of SCC and adenosquamous carcinoma (ASC) in the liver\(^3,5,9,10\): 1) squamous metaplasia in a preexisting AC; 2) squamous metaplasia of the bile duct epithelium or biliary cyst before malignant transformation; 3) divergent differentiation from the bile duct epithelium towards AC and SCC; 4) anaplastic carcinoma differentiating into AC or SCC; and 5) malignant transformation of a hepatic teratoma.

Primary SCC of the liver has also been reported in association with hepatolithiasis, although the etiology of the stones was not revealed\(^3\). Once stones form, they might irritate the lining of the large intrahepatic ducts, causing squamous cell metaplasia, which could in turn progress to SCC.

This is a case report of SCC of the liver that was found without associated hepatic or biliary disease such as a hepatic cyst, adenoma formation, hepatic teratoma, or hepatolithiasis.

Takashi et al.\(^1\) found the CK expression useful for identifying the origins of tumors, as well as for differentiating between primary and metastatic carcinoma of the liver: 1) both the AC and SCC components are positive for CK7 and CK19, which is specific for the bile duct epithelium in the liver; 2) the SCC components show reduced expression of CK8 and CK18, which is evidence of either a hepatocyte or bile duct epithelium origin; and 3) the SCC components express HMW CK, which indicates squamous cell differentiation. These results suggest that most ASC of the liver develops from a squamous change of cholangiocarcinoma. This hypothesis is supported by the finding that neither squamous metaplasia of the bile duct epithelium nor preexisting or associated biliary cysts were observed within or around the tumor in our case, or by the previous report by Lemura\(^7\).

Our patient’s tumor expressed CK19, which occurs in both AC and SCC components, CEA, which is more specific for cholangiocarcinoma than hepatocellular carcinoma (HCC), and HMW CK, which is specific for SCC. It did not express CK8 or CK18, which indicate either a hepatocyte or bile duct epithelium origin, or HAS, which is specific for HCC. Therefore, we concluded that this tumor originated from hepatocytes directly, and not from squamous metaplasia of the bile duct epithelium, a biliary cyst, preexisting AC, or malignant transformation of a hepatic teratoma or hepatolithiasis.

No therapeutic guidelines for primary SCC of the liver have been established. When SCC of the liver is diagnosed, a partial hepatectomy is usually performed, although there is no proven effective therapy and the prognosis is grave\(^12,13\). One reported case of primary SCC of the liver showed a marked response to arterial injection of an anticancer drug\(^4\).

Our patient was first diagnosed with primary SCC of the liver in September 2004. The patient was alive 7 months after undergoing a left lobectomy of the liver and wedge resection of the stomach. Postoperatively, she was given one cycle of intravenous chemotherapy with cisplatin and 5-fluorouracil. However, she could not tolerate the chemotherapy due to nausea, vomiting, and leukopenia. Subsequently, she was treated with oral 5-fluorouracil.

Seven months after the initial diagnosis, the cancer recurred at the surgical site. She developed a malignant pleural effusion in the left lower lung and constant abdominal pain that required narcotic analgesics.

Ours and the reported cases reveal the difficulty in making a correct preoperative diagnosis. The clinical diagnosis of primary SCC of the liver is usually delayed because the symptoms of epigastric pain and weight loss are insidious\(^3\). CT is one of the most valuable preoperative investigations.

Usually, survival from the time of diagnosis does not exceed 1 year, regardless of the treatment, although one patient survived for 16 months after a laparotomy\(^2\). ASC of the liver behaves more aggressively and has a poorer prognosis after hepatic resection than cholangiocarcinoma from other sites\(^11\). We hypothesize that the more SCC components present in the primary tumor, the poorer the prognosis. More case studies are needed to substantiate this.

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