Primary squamous cell carcinoma of the liver: a case report

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INTRODUCTION

Squamous cell carcinoma (SCC) is usually found in skin, rectum, cervical or inguinal lymph nodes. It accounts for 4 to 5 percent of cancer of unknown primary sites. However, primary squamous cell carcinoma of the liver is very rare. Since Imai first reported hepatic teratoma in 1934, about 20 cases have been reported in Korea. Primary SCC of the liver is known to be associated with hepatic cysts and intrahepatic stones. A 71-year-old male was admitted to our hospital, and a abdominal computed tomography scan revealed a 10 × 6 cm mass in the liver. Analysis of a biopsy sample suggested SCC, and so our team performed a thorough workup to find the primary lesion, which was revealed hepatoma as a pure primary SCC of the liver with multiple distant metastases. The patient was treated with one cycle of radiotherapy, transferred to another hospital for hospice care, and then died 1 month after discharge.

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CASE REPORT

A 71-year-old male presented in September 2014 with right flank pain, 10 kg weight loss over past 1 month. He had a past medical history of gout, but no past surgical history. The patient was a current smoker with a 20-pack-year smoking history and chronic alcoholics, with a 0.5 bottle per day, over 40 yrs. He had no prior liver insult. Physical examination revealed no specific finding. He did not have any risk factors for primary SCC of the liver. He was later transferred to another hospital for hospice care, and then died 1 month after discharge.

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have palpable lymph nodes on the head, neck, and inguinal area. There was no suspicious skin lesion. Digital rectal examination was negative, and no perirectal mass or lesion was found. Breathing sound was clear without wheezing or crackle.

Initial vital sign was non-specific (blood pressure 110/70 mmHg, pulse rate 70/min, respiratory rate 20/min, body temperature 36.3°C). Laboratory work-up showed an elevated alkaline phosphatase (ALP)/Gamma-guanosine triphosphate (r-GTP) level of 345/245 IU/L. But total bilirubin 0.44 mg/dL, serum glutamic oxaloacetic transaminase (AST) 22 IU/L and serum glutamic pyruvic transaminase (ALT) 27 IU/L level were within normal limits. Complete blood count showed leukocytosis with neutrophilia (WBC 14,800/mm³, segmented neutrophil 79.5%), anemia (Hemoglobin 10.2 g/dL) and thrombocytosis (Platelet 485 ×10³/mm³). Hepatitis viral markers were all negative, and Ca 19-9 level was slightly elevated (28.58 U/mL). Alpha fetoprotein (AFP) 1.38ng/mL, protein induced by vitamin K absence or antagonist II (PIVKA-II) 55 mAU/mL, carcino-embryonic Antigen (CEA) level were 4.45 ng/mL, all of them were within normal limits.

A computed tomography (CT) scan of the abdomen and pelvis revealed a 10 × 6 cm lobulating contoured low-attenuation mass involving segment VIII and the left lobe of the liver that invaded the left portal vein and bile duct with delayed fill-in enhancement (A: precontrast phase, B: arterial phase, C: portal phase, D: delayed phase).

Figure 1. A computed tomography (CT) scan of the abdomen and pelvis revealed a 10 × 6 cm lobulating contoured low-attenuation mass involving segment VIII and the left lobe of the liver that invaded the left portal vein and bile duct with delayed fill-in enhancement (A: precontrast phase, B: arterial phase, C: portal phase, D: delayed phase).

Figure 2. In the portal phase, tumor thrombi extended into the right atrium via the inferior vena cava (arrow).
vein and bile duct. Unlike primary hepatocellular carcinoma, liver mass showed delayed fill-in enhancement pattern, which mimics cholangiocarcinoma, rather than primary hepatocellular carcinoma (Fig. 1). But Tumor thrombi was invading the middle hepatic vein, extending to the right atrium via inferior vena cava, which was unusual finding for mass-forming cholangiocarcinoma (Fig. 2).

Also, there were multiple metastatic lymphadenopathy involving porta hepatis, portocaval, retrocaval and paraaortic space, with benign-looking multiple cysts in both kidneys, 2.2 cm cyst in the uncinate process of pancreas.

**Figure 3** Chest CT revealed a 3.7 cm osteolytic change mass lesion with destruction of the right 9th rib, with osteolytic change (arrow). There was no parenchymal disease, mediastinal, hilar, or axillary lymphadenopathy. There was also no other primary lesion evident in the chest CT scan. CT, computed tomography.

**Figure 4** Positron-emission tomography–CT showed an intense hypermetabolic mass involving the left hepatic lobe and segment VIII. There were metastatic lymph nodes in the porta hepatis, portocaval, aortocaval, para aortic, and left common iliac spaces, and a small hypermetabolic lymph node in the left supraclavicular area, suggesting distant metastasis. CT, computed tomography.

**Figure 5** (A) The infiltrative tumor was composed of irregular, often interconnected nests of well-demarcated polygonal and squamoid cells. Normal liver parenchyma and glandular structure were not identified. (B) The infiltrative tumor comprised cells with varying degrees of differentiation and varying degrees of cytologic atypia. Larger cells were polygonal and had prominent nucleoli (arrows). Keratin material was not evident. These features can present in poorly differentiated adenocarcinoma or squamous cell carcinoma (A: H&E stain, ×200; B: H&E stain, ×400).
Non-enhanced Chest CT from other hospital showed metastasis to the right ninth rib and surrounding paravertebral soft tissue with osteolytic change (Fig. 3). As mass size was huge and showed the aggressive form, we decided to perform positron emission tomography-CT (PET-CT) for evaluating disease extent. Additionally, PET-CT scan revealed a small hypermetabolic lymph node in the left supraclavicular area, which was suspected as metastatic lesion (Fig. 4). Excisional biopsy on supraclavicular lymph node returned negative. In turn, we had to perform an ultrasonography guided needle biopsy of the liver for pathologic confirmation. Pathology of the liver mass showed infiltrating feature with squamoid shaped cells with varying degrees of differentiation and atypia, which suggests tumor mass as poorly differentiated adenocarcinoma or squa-

Figure 6. Immunohistochemical staining for the malignant, invasive lesion. Hep Par 1 and CK20 stains were negative for the lesion, while CK7, CK19, and P63 stains were positive (All ×200). Hep Par 1, Hepatocyte Paraffin 1; CK, cytokeratin.
mous cell carcinoma (Fig. 5). Immunohistochemistry and special staining for needle biopsy specimens were positive for cytokeratin (CK) 7, 8, 19, and p63. And anti-hepatocyte was negative, suggesting tumor as primary or metastatic squamous cell carcinoma of the liver (Fig. 6).

The patient underwent an extensive workup to search for a primary squamous carcinoma lesion, including neck CT, chest CT, duodenoscopy, sigmoidoscopy, laryngoscopy and ENT survey, all of which turned out to be negative. Taken together, we concluded the tumor as a primary SCC of the liver.

During the hospital day, patient presented uncontrolled high and recurrent fever, which was suspected to be the cancer fever. Patient’s general condition continued to get worsen. First, we considered palliative chemotherapy, however we failed to conduct due to his poor general condition (Eastern Cooperative Oncology Group 3). The patient started palliative radiotherapy for right paravertebral mass. After 10 times of radiation therapy, patient refused further treatment and transferred to the local hospital for hospice care, and passed away about a month after discharge.

DISCUSSION

Primary SCC of the liver has been reported to be associated with hepatic cyst, intrahepatic stone, liver cirrhosis, and Caroli’s disease, but true mechanism of tumor formation is still uncertain. The incidence of primary SCC of the liver is extremely low, and its pathogenesis and therapeutic guideline has not been settled. Its clinical course is aggressive and hard to achieve more than 1-year-survival. Many articles suggest that primary SCC of the liver is associated with benign hepatic cysts, but its exact steps leading up to the carcinomas are not proven yet. Several articles propose that a squamous epithelium lining benign cysts undergo dysplasia-metaplasia sequence, and ultimately, become malignant SCC.

In this case, the existence of hepatic cysts before formation of squamous cell carcinoma is not clear. Carrim reported that patients with either renal or hepatic cysts have a greater chance of having the other compared with baseline prevalence. As the patient has multiple benign cysts on kidney, we suspect that hepatic cysts could have been present before cancer formation. Also, expression of biliary CK 19 on pathology supports the pre-existence of biliary epithelial cells and its transformation of malignancy. The examination to find the primary site of the SCC including ENT examination turned out to be negative. Overall, the liver mass should be considered primary SCC of the liver.

According to the past studies, patients with primary SCC of the liver may present various symptoms including abdominal pain or discomfort, jaundice, weight loss, loss of appetite, and rarely, progressive dysphagia. Thorough physical examination might be able to find palpable abdominal mass and tenderness over right upper quadrant, with fever.

Several methods including surgical resection, chemotherapy, radiotherapy, Transcatheter arterial chemoembolization has been reported for treatment of primary SCC of the liver. Like most of the hepatic malignancy, surgical resectability and operability is one of the most important factors deciding prognosis. If surgical resection could be performed before tumor invading surrounding liver parenchyma, this could lead to a good prognosis. Weimann et al performed surgical resection for primary SCC of the liver, without any adjuvant chemotherapy or radiation therapy, and patient survived more than 4 years. Banbury et al also performed surgical resection for primary SCC of the liver, and patient survived more than 16 months without any adjuvant therapy. But most of the cases of primary SCC of the liver are advanced, surgical resection alone cannot promise good prognosis and improve overall survival, and that radiation therapy or chemotherapy with 5-FU and/or CDDP should be considered with complete surgical resection. Boscolo et al. reported to have successfully treated advanced primary SCC of the liver with systemic CDDP and 5-FU therapy with surgical resection. In the present study, therapeutic regimes were largely limited as the patient’s general physical condition was too fragile to tolerate systemic chemotherapy, and the tumor had been already metastasized to various parts of the body including abdominal lymph nodes and rib. There was no clear benefit for surgical resection, too. Considering the patient’s performance status and advanced tumor burden, we performed local radiotherapy to relieve symptoms. The patient expired 1 month after discharge, in the hospice care center.

In summary, primary SCC of the liver is a very rare cancer, which requires thorough and complete examination for the diagnosis. After systemic examination for excluding all the other possible primary sites including skin, rectum, cervical or inguinal lymph nodes, we should consider hepatoma as primary SCC of the liver, only when ample and adequate biopsy specimens present squamous cell feature. As the treatment guideline has not been settled, clinician should choose the treatment...
modality based on patient’s clinical status, and various therapy including surgery, chemotherapy and radiotherapy for remission and better prognosis.

Conflicts of Interest
The authors have no conflicts to disclose.

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