Gastroenterology and Hepatology From Bed to Bench.

CASE REPORT

Primary squamous cell carcinoma of the liver: a case report

Hamid Rezvani[1], Hamed Azhdari Tehrani[1], Sina Salari[1], Selda Feiziazar[2], Maryam Darnahal[1]

[1] Department of Hematology-Medical Oncology, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2] Department of Pathology, Emam Hossein Hospital, Shahid Beheshti University of Medical Science, Tehran, Iran

ABSTRACT

Primary squamous cell carcinoma (SCC) of the liver is rare and has an extremely poor prognosis. It is very difficult to detect and is sometimes misdiagnosed. It has been reported that male sex, hepatic cyst, hepatolithiasis, hepatic teratoma, and liver cirrhosis may be associated with SCC of the liver. A 67-year-old woman was admitted to our hospital with anorexia, weakness, and right upper quadrant abdominal (RUQ) pain. Sonography and an abdominal computed tomography scan revealed a 36 × 34 cm mass in the liver. Pathological analysis of the sample suggested SCC. According to the negative radiographic findings in other major organs, the tumor was considered primary. The patient was treated with surgical resection and followed by palliative care. Our case died 5 months after the initial presentation.

Keywords: Squamous cell carcinoma, Liver, Case report, Treatment, Diagnosis, Pathology.

(Please cite as: **Rezvani H, Azhdari Tehrani H, Salari S, Feiziazar S, Darnahal M. Primary squamous cell carcinoma of the liver: a case report. Gastroenterol Hepatol Bed Bench 2022;15(4):430-434. https://doi.org/10.22037/ghfbb.v15i4.2476).**

Introduction

Squamous cell carcinoma (SCC) occurs in areas of the body covered by squamous epithelium such as the rectum, skin, and cervical or inguinal lymph nodes. Because there are no squamous epithelial cells in the liver, primary squamous cell carcinoma is exceedingly rare in this location (1, 2). Since 1970, only dozens of such cases have been reported in the English literature (2, 3), and their true histological source is controversial. It has been reported that they have not originated directly from liver tissue, but from either the lining of a developmental hepatic cyst or tumor transformation of the biliary epithelium (2, 4). It has been reported that male sex, hepatic cyst, hepatolithiasis, solitary benign non-parasitic hepatic cysts (SBNHC), hepatic teratoma, and liver cirrhosis are possibly associated with SCC of the liver; however, sometimes patients did not have a prior liver insult or known risk factors (4-7). Because of the lack of specific clinical and imaging characteristics, diagnosis is difficult and sometimes made in error (1, 3). Despite a variety of treatment options constituting surgical resection, liver transplantation, radiotherapy, interventional local chemotherapy, and radiofrequency ablation, patients usually do not respond to treatment and have an extremely poor prognosis with overall survival of fewer than 12 months, even after treatment (1, 6). This report presents a case of primary SCC of the liver with no history of liver insult, cancer, or known risk factors.

Case report

A 67-year-old woman with a history of diabetes and hypertension was admitted to our hospital in January 2021 with anorexia, weakness, right upper quadrant abdominal (RUQ) pain, and a 10-kg weight loss over the past 1 to 2 months. She did not drink alcohol nor smoke, and she had no history of liver insult or cancer. On physical examination, jaundice was detected, but the liver and spleen were not palpable. The patient did not have palpable lymph nodes on the neck, head, or

Received: 18 June 2022 *Accepted*: 27 August 2022
Reprint or Correspondence: **Maryam Darnahal,** *Department of Hematology-Medical Oncology, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*
E-mail: maryamdarnahal@yahoo.com
ORCID ID: 0000-0001-9376-2554

inguinal area. Hematological analysis was normal (Table 1).

Table 1. Summarize patient information.

Variable	Patient
Gender	female
Age, y	67
Liver cyst	-
Hepatolithiasis	-
ALT/AST, U/L	14/23
BILI T/BILI D, mmol/L	0.5/0.3
AFP/CEA, ng/mL	0.5/1.6
ALP, U/L	251
CA 19-9, U/ml	5.3
CA- 125, U/ml	32.7
Tumor size, mm	36 × 34 mm
Tumor number	Single
Tumor location	Segments IV and V of the right lobe
Primary Treatments	Right lobe hepatectomy
Survival time, months	5
Outcome	dead

Abbreviations: AST, aspartate transaminase; ALT, alanine aminotransferase; BILI T, total bilirubin; BILI D, direct bilirubin; AFP, alpha-fetoprotein; CEA, aspartate transaminase; ALP, Alkaline phosphatase: CA, cancer antigen.

Sonography results revealed a 36 × 34-mm mass in the distal common bile duct (CBD) between segments 4 and 5 of the right lobe of the liver with invasion of the right hepatic artery and right portal vein. A computed tomography (CT) scan of the abdomen and pelvis with contrast was also done and confirmed the same mass in the liver. No other mass was observed in the abdomen o pelvis (Figure 1A). Lung computed tomography was also normal.

The initial diagnosis was hepatocellular carcinoma (HCC) and right lobe hepatectomy was performed. Immunohistochemical analysis of the liver mass showed that the tumor cells were negative for hepatocyte paraffin-1 (HepPar-1), the HCC marker. Cytokeratin (CK)7, 8, 18, 20 (-) and gross cystic disease fluid protein (GCDFP-15) were negative, but P63 was positive (Figure 2). Hematoxylin-eosin staining (H&E) of the liver mass showed infiltrating features with squamoid cells and varying degrees of

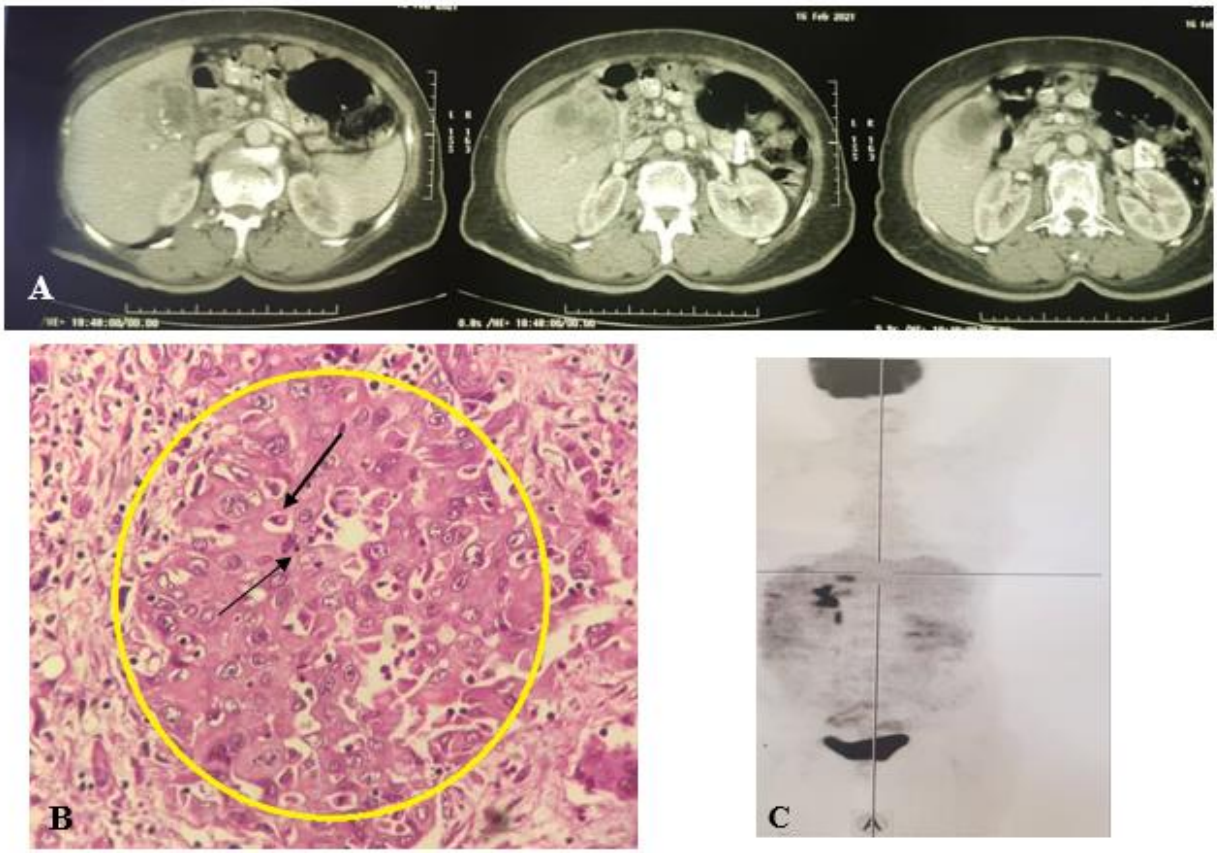

Figure 1. Image characteristics in the present case. CT- scan of the abdomen and pelvis revealed a mass with a size of 36×34 mm in the distal common bile duct (CBD) between segments 4 and 5 of the liver (A). Microscopically (hematoxylin and eosin (HE) 100), the tumor is composed of squamous cells with nonkeratinization (B). Positron emission tomography-computed tomography showed a hypermetabolic mass with a size of 26×28 mm involving the edge of the lobectomy site (C).

differentiation and atypia (Figure 1B). According to the immunohistochemistry and staining results, the diagnosis of hepatocellular carcinoma was rejected, and metastatic moderately differentiated nonkeratinizing squamous cell carcinoma was confirmed. Upper endoscopy and pap smear test were done, but no malignancy was observed. Because of the patient's abdominal pain, a positron emission tomography (PET) scan was performed six weeks after surgery that showed a hypermetabolic mass 26×28 mm in size involving the edge of the lobectomy site with SUVmax=10.8, indicating recurrence (Figure 1C). Because of the patient's condition, no reoperation or chemotherapy was performed, and palliative care was recommended. The patient died 5 months after the initial presentation.

Discussion

Primary hepatic squamous cell carcinoma is extremely rare with high malignancy (1, 2). It has a poor prognosis and average survival time of the patient is less than 12 months (2, 3). A review of literature from 1997 to 2016 showed the median overall survival and disease-specific survival for this patients was 7.7 months and 2.0 months, respectively (3). Patients with primary SCC of the liver were admitted with common symptoms, including pain in the right upper region of the abdominal, loss of appetite and weight, jaundice, and progressive dysphagia (4, 6). In this case, the initial diagnosis was HCC, and a right lobe hepatectomy was performed. Immunohistochemically, our case was positive for p63 and negative for CK7, CK20, CK18, CK8, HepPar-1, and GCDFP-15. It is known that primary SCC of the liver is positive for p63 (3, 8). In addition, H&E staining of the liver mass showed infiltrating features with squamoid-shaped cells and varying degrees of differentiation and atypia. Based on IHC and H&E results, the diagnosis of HCC was

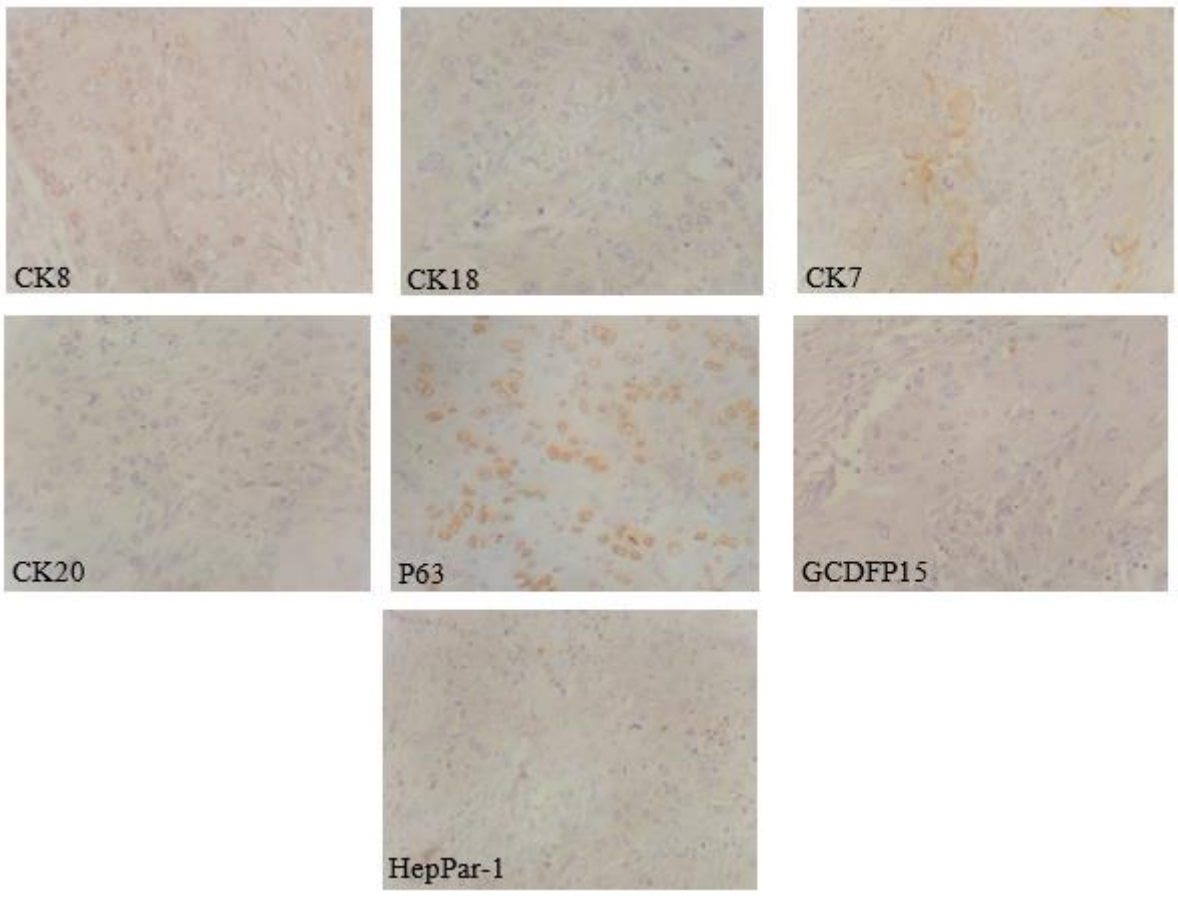

Figure 2. IHC analysis showed that CK8, CK18, CK7, CK20, GCDFP-15, and HepPar-1 staining were negative, but p63 expression was positive.

rejected, and SCC was confirmed. Radiographic analyses including enhanced CT and MRI help determine the location of primary tumors and add useful information involving the number of lesions, their size and extent, and the degree of tumor invasion. The diagnosis of primary SCC of the liver is to exclude metastatic SCC of the liver from other primary sites (3, 9). In the present study, to preclude the primary site of SCC, a gynecological examination and lung, thyroid, esophagus, abdomen, pelvic, and gastrointestinal tract CT scans were performed. CT scans, postoperative pathology and immunohistochemistry findings confirmed the SCC as liver primary squamous cell carcinoma. There are various theories about the pathogenesis of primary SCC, including hepatic cyst, intrahepatic bile duct stones, liver cirrhosis, chronic cholangitis, congenital biliary cyst, solitary benign non-parasitic hepatic cysts (SBNHC), hepatic teratoma, and Caroli's disease; similar to our case, however, the exact mechanism of tumor formation remains unclear (4-6, 10). In primary liver SCC, changes in liver function such as increased levels of ALT, AST, BILI T, and BILI D, are usually observed (2). It is known that this dysfunction is associated with chronic inflammation of bile ducts, liver cyst, and cancer invasion or cancer-related obstruction of the bile duct (3). In the case reported herein, the patient had no history of liver insult or cancer, and the ALT, AST, BILI T, and BILI D levels were normal. In confirmation of our data, some studies have reported that patients do not always have a prior liver insult or known risk factors for primary SCC of the liver (4). It has also been reported that liver pluripotent stem cells may transform into cancerous tissues containing squamous cells, hepatocytes, and biliary epithelial cells under the action of various carcinogenic factors, with the cells then developing into squamous cell carcinoma (1, 2). Therefore, it is possible that in the present case, squamous cell carcinoma originated from pluripotent stem cells.

There are several treatment protocols for this condition, including surgical resection, liver transplantation, radiotherapy, interventional local chemotherapy, and radiofrequency, but there is no standard care for primary SCC of the liver (3). Patients usually do not respond to treatment and have an extremely poor prognosis with an overall survival of less than 12 months, even after treatment (1, 6). In previous case series and literature reviews, 40.1% of patients who underwent surgery resection survived over 12 months, and patients with radical surgery treatment had a longer overall survival rate compared to those with palliative treatment (median overall survival: 17 versus 5 months) (2). Weimann et al. performed surgical resection without adjuvant chemotherapy or radiation therapy, and their patient survived more than 4 years (11). In some cases, the SCC is advanced, and surgery alone is not helpful; radiation therapy or chemotherapy should be considered with complete surgical resection (9). In the present case, the tumor recurred 6 weeks after the patient's first surgery. It has been suggested that if the tumor recurs, re-hepatectomy, systemic chemotherapy, or hepatic arterial infusion of low-dose chemotherapy could be performed (8, 9). In the present case, therapeutic options were largely limited, as the patient's general physical condition was too fragile to tolerate systemic chemotherapy. Therefore, palliative care was recommended. The patient died 5 months after the initial visit.

Conclusion

In summary, primary SCC of the liver is a very rare malignancy difficult to diagnose; therefore, it needs thorough and complete examination. After systemic examination to exclude other possible primary sites, such as the skin, rectum, lung, thyroid, esophagus, abdomen, pelvic, gastrointestinal or inguinal lymph nodes, we should consider hepatoma as primary SCC of the liver based only on IHC and pathology findings. It is necessary to increase our knowledge about this disease in clinical practice to avoid misdiagnosis and to identify the best treatment.

Conflict of interests

The authors declare that they have no conflict of interest

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