Primary Squamous Cell Carcinoma of Liver
Case Series and Review of Literatures

Xu-Feng Zhang, MD, PhD, Zhao-Qing Du, MD, Xue-Min Liu, MD, and Yi Lv, MD, PhD

Abstract: Primary squamous cell carcinoma (SCC) of liver is rare, and its prognosis is extremely poor. This study aims at reviewing the clinical data of all pathologically diagnosed liver cancer in our institute, and discussing the clinical presentation, diagnosis, treatment, and prognosis of our cases of SCC and the literatures reported previously.

All the patients undergoing liver surgery or biopsy for liver cancers from 2002 to 2013 in our hospital were reviewed, and the liver specimens were examined pathologically. A literature search for case reports of primary SCC of liver published until December 31, 2014, was performed on PubMed, MEDLINE, Scopus Elsevier, Cochrane, and Google Scholar. The primary data of the case reports were all included and analyzed if available.

From January 2002 to October 2013, 2210 cases of liver cancer were diagnosed pathologically in our hospital. Among, 4 cases (0.2%) were diagnosed as primary SCC of liver. All were negative for hepatitis B infection, but present with liver cyst and/or hepatolithiasis. One patient underwent radical resection, but died of tumor recurrence 18 months postoperatively. One patient received transcatheter arterial chemoembolization and 1 patient received laparotomy and alcohol injection, but died 9 and 4 months after surgery, respectively. The last patient received only biopsy and supportive treatment, and finally died of tumor metastasis 6 months later. From 1970 to 2014, 31 cases of primary liver SCC have been published in English previouslly. Thirty one cases and the 4 cases in the present study were included. The average age of the patients were 54 years (range 18–83), with a male to female ratio of 19:16. Twenty patients had liver cysts, 7 had bile duct stones, and 2 cases had both. Patients undergoing radical surgery had better prognosis than those undergoing palliative treatments (median survival 17 vs 5 months, \( P = 0.005 \), log-rank test). Patients with liver cysts seemed to have worse prognosis than those with bile duct stones (median survival 7 vs 18 months, \( P = 0.090 \), log-rank test).

Primary liver SCC seems to be mostly originated from liver cyst or hepatolithiasis. Radical surgery should be firstly recommended, although the prognosis might be unfavorable.

INTRODUCTION

Primary squamous cell carcinoma (SCC) of liver is rare and only reported sporadically. To our knowledge, only 31 cases have been reported in English literatures since 1970s. Primary SCC of the liver has been mostly reported to be associated with hepatic cyst, hepatolithiasis, or hepatic teratoma.\(^1\)\(^{-27}\) Although it has been proposed that SCC of liver is originated from tumor transformation of biliary epithelium under chronic inflammation or metaplastic and subsequent neoplastic transformation of pre-existing cysts of the liver, the true mechanism remains unknown.\(^1\)\(^{-27}\) The prognosis of this tumor is extremely poor, only a few patients survived more than 12 months even after treatment as reported.\(^10,12,23\)\(^{-26,28,29}\) Therefore, primary liver SCC is extremely rare occurred and different from other primary liver cancers.

Herein, we reported 4 cases of primary SCC of liver treated in our hospital over a period of 12 years. And we also summarized and analyzed the clinical details of the cases reported in English literatures.

PATIENTS AND METHODS

Patients

The clinical data of the patients diagnosed with primary liver cancer were collected retrospectively from January 2002 to October 2013. Totally, there were 11,154 cases of primary liver cancer admitted to our hospital during the period. Among, 2210 patients were confirmed pathologically of primary liver cancer. The results of pathological examination of the tumors were reviewed. Four patients (0.2%) were diagnosed as primary SCC of liver. The slides with the tissue section of SCC were obtained and reviewed by 2 pathologists independently. Laboratory data of the patients were documented before the treatments. The imaging data available of the patients were evaluated by at least 2 radiologists. After the discharge, the patients were followed up every 6 months till death. This study was approved by the Ethic Committee of the First Affiliated Hospital, Xi’an Jiaotong University, China. And the use of the patient’s data anonymously was informed to the patient’s family, and was consent by them.
Literature Review
A systematic review of the SCC of liver was performed by searching electronic databases (Pubmed, Web of Science, MEDLINE, Cochrane Library, and Google Scholar) prior to October 2014 with English language. Each case of the reports were documented as first author, publication year, patient’s age, gender, comorbidities, tumor status, treatments, and survival time.

RESULTS

Case Series

Case 1
An 83-year-old man presented with anorexia, nausea, right upper quadrant abdominal pain, and a 10-kilogram weight loss over the past 1 to 2 months. He had a history of liver cyst for 5 years and severe chronic obstructive pulmonary disease for 20 years. Hematological analysis revealed increased white blood cells. Liver function was normal (Table 1). The value of alpha fetoprotein (AFP) was normal but carcinoembryonic antigen (CEA) was slightly elevated. Enhanced computed tomography (CT) revealed a large predominantly cystic mass in the right lobe of the liver (5 cm × 5 cm), which was unevenly enhanced at arterial phase but slightly retrieved at venous phase. And also, multiple round low-density lesions were presented in the liver, which was not enhanced at either phase (Figure 1A, B).

An ultrasonography (US)-guided fine needle aspiration biopsy of the mass returned positive for SCC (Figure 1C, D) composed of squamous cells with keratinization (arrowhead). Clinical, chest CT and gastrointestinal radiography evidenced negative findings in the case. Therefore, the final diagnosis of primary SCC of liver was made. However, due to the severely poorer pulmonary function and general condition of the patients, his families refused any aggressive treatment. The patient received transcatheter arterial chemoembolization (TACE). Angiography through hepatic artery showed multiple nodular tumors dyeing, which was weak centrally but strong peripherally, in the right lobe (Figure 2B, C). The hybrid emulsion with 5-fluorouracil (1.5 g), cisplatin (40 mg), adriamycin (60 mg), and lipiodol (15 mL) was injected via the catheter selectivity to the right hepatic artery, followed by embolization with polyvinyl alcohol microsphere. The patient received additional TACE 1 and 3 months later, and no nodular tumor dyeing or collateral vessels of right hepatic artery were identified. The patient was then treated with SOX chemotherapy regimen (Oxaliplatin 200 mg, day 1, and S-1 50 mg, b.i.d. day 1–14) at 4th and 6th month. However, the patient was found tumor thrombus in common bile duct and lung metastasis 6 months after the first TACE, and then died 3 months later.

Case 2
A 70-year-old man was seen in our department, complaining of blunt pain in right upper abdomen with nausea and vomiting for 10 days. US of the local hospital identified multiple large cystic mass in the liver. She has no history of hepatitis B virus infection. After admission, liver function tests showed slightly elevated alanine aminotransferase (ALT), aspartate transaminase (AST), total bilirubin, and direct bilirubin (Table 1). But the values of AFP and CEA were normal. Enhanced CT revealed multiple low density lesions in the right and left lobes with slightly uneven enhanced edge at arterial phase, and further enhanced at portal venous and parenchymal phase, which, however, was still lower than that of liver parenchyma (Figure 2A).

A US-guided percutaneous liver puncture was undertaken, and SCC was examined microscopically (Figure 2D, E). The patient had no lesions in lungs, gastrointestinal tract, uterus, or ovaries. Therefore, primary SCC of liver was diagnosed. The patient received transcatheter arterial chemoembolization (TACE). Angiography through hepatic artery showed multiple nodular tumors dyeing, which was weak centrally but strong peripherally, in the right lobe (Figure 2B, C). The hybrid emulsion with 5-fluorouracil (1.5 g), cisplatin (40 mg), adriamycin (60 mg), and lipiodol (15 mL) was injected via the catheter selectively to the right hepatic artery, followed by embolization with polyvinyl alcohol microsphere. The patient received additional TACE 1 and 3 months later, and no nodular tumor dyeing or collateral vessels of right hepatic artery were identified. The patient was then treated with SOX chemotherapy regimen (Oxaliplatin 200 mg, day 1, and S-1 50 mg, b.i.d. day 1–14) at 4th and 6th month. However, the patient was found tumor thrombus in common bile duct and lung metastasis 6 months after the first TACE, and then died 3 months later.

Case 3
A 50-year-old man was seen in our department, complaining of mild fever and pain in the right upper quadrant of the abdomen for half a year. The patient had a history of cholecystectomy about 20 years ago due to cholecystolithiasis. Physical examination revealed deep tenderness in the upper abdomen. Hematological analysis revealed mild hypochromic anemia and increased white blood cells. Liver function test showed slight increase in ALT, AST, alkaline phosphatase, and CEA. A US-guided percutaneous liver puncture was undertaken, and SCC was examined microscopically (Figure 2D, E). The patient had no lesions in lungs, gastrointestinal tract, uterus, or ovaries. Therefore, primary SCC of liver was diagnosed. The patient received transcatheter arterial chemoembolization (TACE). Angiography through hepatic artery showed multiple nodular tumors dyeing, which was weak centrally but strong peripherally, in the right lobe (Figure 2B, C). The hybrid emulsion with 5-fluorouracil (1.5 g), cisplatin (40 mg), adriamycin (60 mg), and lipiodol (15 mL) was injected via the catheter selectively to the right hepatic artery, followed by embolization with polyvinyl alcohol microsphere. The patient received additional TACE 1 and 3 months later, and no nodular tumor dyeing or collateral vessels of right hepatic artery were identified. The patient was then treated with SOX chemotherapy regimen (Oxaliplatin 200 mg, day 1, and S-1 50 mg, b.i.d. day 1–14) at 4th and 6th month. However, the patient was found tumor thrombus in common bile duct and lung metastasis 6 months after the first TACE, and then died 3 months later.

TABLE 1. Summary of 4 Patients With Primary Squamous Cell Carcinoma of Liver

| Case 1 | Case 2 | Case 3 | Case 4 |
|---|---|---|---|
| Gender | Male | Female | Male | Female |
| Age, y | 83 | 70 | 50 | 73 |
| HbsAg | + | + | + | + |
| Liver cyst | + | + | + | + |
| Hepatolithiasis | - | - | - | - |
| ALT/AST, U/L | 27/13.5 | 101/90 | 33/41 | 17/29 |
| TBIL/DBIL, µmol/L | 8.7/2.4 | 32.9/15.3 | 22.8/14.6 | 8.2/2.6 |
| AFP/CEA, ng/mL | 2.9/16.8 | 1.8/0.6 | 6.7/26 | N/A |
| Tumor size, cm | 10 | 15 | 7 | 11 |
| Tumor number | Single | Multiple | Single | Multiple |
| Tumor location | IV/V/VIII | IV/V/VI/VII/VIII | II/III/IV | Whole liver |
| Primary Treatments | Biopsy and supportive treatment | Biopsy, TACE, and chemotherapy | Left hemihemipatectomy, choledochojejunostomy | Alcohol and fluorouracil injection |
| Survival time, ms | 6 | 9 | 18 | 4 |
| Outcome | Dead | Dead | Dead | Dead |

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bilateral value. Virologic markers for hepatitis were negative. A normal value of AFP but increased value of CEA was documented after admission (Table 1). An abdominal CT scan demonstrated multilocular cystic lesions with diameter of 7 cm. The edge and interval between the lesions were slightly enhanced at arterial phase, which did not exit at portal venous. The intra- and extrahepatic bile ducts were dramatically dilated with high-density lesions in the ducts, which were not enhanced at both phases (Figure 3A, B). Intrahepatic cholangiocarcinoma was suspected with intra- and extrahepatic bile duct stones.

At laparotomy, a large lesion involving the left lobe of the liver was discovered. Parts of the cystic wall were pale and necrotic, and intraoperative histopathological examination of the frozen specimen suggested malignant lesions with marked pleomorphism cells. A left hemihepatectomy with hepato- and choledocho-lithotomy and then choledochojejunostomy was performed. There were no residue stones in the bile ducts checked by fibercholeochoscope. And R0 resection was confirmed by histological findings. Final histology revealed primary SCC of liver (Figure 3C, D), which was negative for alpha-fetoprotein staining immunohistochemically (Figure 3E). The strong positive staining of CK 14 and CK 56 indicated basal cells of keratinized squamous epithelium origin of the cancer cells (Figure 3F, G). The positive expression of CK19 confirmed the bile ductular ontogeny of the neoplastic cells (Figure 3H). The patient recovered well and was discharged 7 days postoperatively. However, the patient died of tumor recurrence 18 months after the initial presentation.

**Case 4**

A 73-year-old woman presented with 10-year history of intermittent right upper abdominal pain but persistent and exacerbated for 2 weeks. The previous disease record revealed multiple liver cyst and gallbladder muddy stones of the patients, but no treatment had been given before the admission to our hospital. There was no jaundice, fever, or weight loss. No renal or pancreatic cyst could be found. Physical examination revealed a palpable edge of the liver with overlying tenderness. The liver function tests were all in normal range (Table 1). US and CT scan showed multiple cystic mass in liver, but some with thick wall (data were unavailable). The patients subsequently underwent laparotomy. Two large cysts were observed with pale and white nodules on the cystic wall. Part of the cystic wall with suspicious nodules was dissected, and sent for fast frozen examination. After that, some soft and brown debris and several yellow-pick stones were observed in the cysts, and suctioned. Fast frozen examination of the nodules on the cystic wall showed SCC. Due to the wide spread of the tumors in the liver and lymph nodes in hepatoduodenal ligament, 4 large cysts were unroofed and injected with 20 mL alcohol and 0.4 g fluorouracil.

Microscopic examination showed cystic wall was lined by squamous epithelium with atypical dysplasia and moderate differentiated SCC (Figure 4). The patient recovered well with relief of the right upper abdominal pain, but the bile-like fluids were drained from the drainage tube 40 to 50 mL/day for a week. The patient was discharged 10 days postoperatively. She died 4 months later of progressive cachexia with dysfunction of liver, lung, and kidneys.

**Prognosis of Primary Liver SCC**

Totally, from 1970 to 2013, 31 case-reports have been published in English with intact information. Thirty five cases of liver SCC were documented and analyzed in the present study including our cases. The average age of the patients were 54 years (range 18–83), with a male to female ratio of 19:16.
Liver cysts and bile duct stones were the most common comorbidities of primary SCC of liver (20 cases with liver cysts, 7 cases with bile duct stones, and 2 cases with both), although there were 3 cases with no recorded disease (Table 2).

The median survival time of all the 32 patients with recorded prognosis was 7.5 months (range 0.3–84 months). Whether treatments, comorbidities or gender has any impacts on survival of patients with primary liver SCC remains unknown. It was obvious that patients undergoing radical surgery had a better prognosis than those undergoing palliative treatments (median survival 17 vs 5 months, $P = 0.005$, log-rank test, Figure 5A). Patients with liver cysts seemed to have worse prognosis than those with bile duct stones, although the difference was not statistically different (median survival 7 vs 18 months, $P = 0.090$, log-rank test, Figure 5B). Gender seemed not to be an impact factor on prognosis of these patients ($P = 0.979$, log-rank test, Figure 5C).

**DISCUSSION**

**Etiology and Pathogenesis**

Various theories have been proposed concerning the pathogenesis of primary liver SCC. Chronic inflammation of the bile duct or congenital cysts of the biliary tract or liver cysts in association with infection and/or stones has been attributed as the major etiological factors. Continuous irritation due to chronic inflammation might promote secondary squamous metaplasia and subsequent malignant transformation.1–27 These also fit with our cases that 2 patients had long history of liver cyst, one had intra-hepatolithiasis and one had both. Together with the published cases of primary liver SCC, 20 cases of patients had coexisting liver cysts, 7 cases had bile duct stones, and 2 cases had both. Therefore, it is possible that “inflammation-cancer” transformation might occur in some patients with liver cyst or bile duct epithelium, and very few of them would develop primary liver SCC. It must be very interesting to establish animal models to mimic the malignant transformation of cyst or bile duct epithelium to squamous carcinomatous epithelium.

It is noticeable that 3 cases reported no coexisting disease, 1 case had mixed hepatocellular and cholangiocarcinoma, and 1 had colon cancer.28–32 It is difficult to find out the pathogenesis of primary liver SCC in these cases. However, it has also been suggested that squamous metaplasia arising from adenocarcinoma cells may have the potential to differentiate into any of a variety of cell types, and liver SCC may occur from...
adenocarcinoma cells, as reported by Tsuneyama et al. In addition, it has also been proposed that primary liver SCC can develop from hepatocytes or intrahepatic cholangiocytes de novo.

Clinical Presentation and Laboratory, Imaging Findings

Blunt pain in the right upper quarter of the abdomen is the most frequent symptoms presented. However, this is not the specific symptom that could distinguish the disease from other liver mass, especially when the patient has known disease record of liver cyst or hepatolithasis. In our cases, all the 4 patients were admitted with complain of abdominal pain. However, in the reported cases, some patients could have some other nonspecific symptoms, such as jaundice, dyspepsia, fever, etc. Most of these patients would show increased serum level of ALT, AST, and even bilirubin, due to chronic inflammation in bile ducts or liver cyst and invasion of the tumors. However, there is a lack of specific serum marker of primary liver SCC at the present time.

CT seems to be the most valuable preoperative investigation. On CT imaging, focal wall thickening of liver cysts or intrahepatic biliary, or irregularity as hemorrhage might be suggestive of malignant changes. However, the diagnosis of primary SCC is still very difficult to make. Firstly, some patients had no obvious liver mass even by CT scan but only liver cyst or hepatolithiasis preoperatively. These patients might be diagnosed intraoperatively or postoperatively by

FIGURE 3. Abdominal computed tomography (CT) shows multilocular cystic lesions and dilated intrahepatic bile ducts with high-density lesions in the ducts (A, B). Microscopic findings of the resected tumor revealed sparse distribution of squamous cell carcinoma with keratinization (HE staining, C, D, arrowhead). Some normal bile ducts could be seen (C, arrows). Squamous cells express negative alphafetoprotein staining, but strong positive CK14, CK 56, and CK 19 staining immunohistochemically (E–H).

FIGURE 4. Microscopic findings of the resected cystic wall revealed squamous cell carcinoma with keratinization (HE staining, A 4×, B 20×, arrowhead).
| Authors                  | Year | Age/Sex | Comorbidities       | Tumor Size/Number/Location          | Treatment                                | Outcome/Survival |
|--------------------------|------|---------|---------------------|------------------------------------|------------------------------------------|------------------|
| Greenwood and Orr         | 1970 | 37/M    | Liver cyst           | 16 cm/single/right lobe             | Laparotomy and biopsy                    | Dead/2 months    |
| Bloustein and Silverberg  | 1976 | 30/M    | Liver cyst           | 8.8 cm/single/right lobe            | Roux-en-Y drainage, extended right lobectomy | Dead/8 months    |
| Song et al               | 1984 | 43/M    | Hepatolithiasis      | 13 cm/single/left lobe             | Left hemihepatectomy                     | Dead/6 months    |
| Gresham and Rue          | 1985 | 78/M    | Liver cyst           | 20 cm/single/portahepatis          | Biopsy                                   | Dead/2 months    |
| Lynch et al              | 1988 | 63/M    | Liver cyst           | 8 cm/single/portahepatis           | Cyst evacuation and T tube drainage in common bile duct | Dead/6 months    |
| Clements et al           | 1990 | 73/M    | Gallstones           | 5 cm/multiple/liver, omentum       | Conservation                             | N/A              |
| Roediger and Dymock      | 1991 | 51/F    | Gallstones           | 6 cm/multiple/liver                | Right hemihepatectomy                    | Died/10 days     |
| Nieweg et al             | 1992 | 62/F    | Liver cyst           | 15 cm/single/whole liver           | Laparotomy                              | Died/5 months    |
| Pliskin et al            | 1992 | 82/F    | Liver cyst           | 4 cm/liver, lung and bone marrow   | Conservation                             | Died/13 days     |
| Banbury et al            | 1994 | 59/F    | Liver cyst           | 14 cm/single/right lobe            | Right hemihepatectomy                    | Survive/16 months|
| Lombardo et al           | 1995 | 74/F    | Liver cyst           | 17.5 cm/single/right lobe          | Right hemihepatectomy                    | Alive/8 months   |
| Weimann et al            | 1996 | 71/F    | Liver cyst           | 16 cm/single/right lobe            | Right hemihepatectomy                    | Alive/4.5 years  |
| Monteaudo et al          | 1998 | 51/M    | Liver foregut        | 12 cm/single/liver, gallbladder,   | Cyst biopsy and drainage                 | Died/1 month     |
| Vicky et al              | 2001 | 21/M    | Liver cyst           | 10 cm/single/right lobe            | Resection of gallbladder, malignant      | Died/2 months    |
| Caratuzzolo et al        | 2002 | 21/M    | Liver foregut cyst   | 10 cm/multiple/liver, transverse   | Right hepatectomy, right hepatectomy and antrectomy | Survive/3 months |
| de Lajarte-Thirouard et al| 2002 | 40/F    | Liver foregut cyst   | 13 cm/single/right lobe            | Right hemihepatectomy                    | Died/2 months    |
| Kaji et al               | 2003 | 67/F    | None                 | 10 cm/multiple/whole liver         | Chemotherapy                            | Died/23 months   |
| Yagi et al               | 2004 | 42/M    | Liver cyst           | 25 cm/multiple/whole liver         | Post-mortem pathological dissection      | N/A              |
| Tsuneiya and et al       | 2005 | 60/M    | Hepatocellular and   | 4 cm/single/right lobe             | Partial hepatectomy                      | N/A              |
| Boscolo et al            | 2005 | 64/M    | Hepatolithiasis      | 10 cm/single/left lobe             | Chemotherapy and resection               | Survive/11 months|
| Odemis et al             | 2006 | 18/M    | Liver cyst           | 5 cm/single/liver                  | Right hepatectomy and Whipple’s procedure | Died/7 months    |
| Lee et al                | 2006 | 40/M    | None                 | 10 cm/single/right lobe            | Extended right lobectomy                 | Survive/9 months |
| Naik et al               | 2009 | 56/M    | None                 | 3 cm/single/left lobe              | Radiation and extended left lobectomy    | Survive/6 months |
| Zhang et al              | 2009 | 60/F    | Liver foregut cyst   | 7 cm/single/left lobe              | Partial hepatectomy                      | Survive/6 months |
| Iimuro et al             | 2011 | 73/F    | Liver cyst           | 10 cm/single/right lobe and lung   | Liver and lung resection, chemotherapy   | Died/13 months   |
| Spaggiari et al          | 2011 | 72/M    | Hepatolithiasis      | 10 cm/single/right lobe            | Right hemihepatectomy                    | Survive/7 years  |
| Zhao et al               | 2012 | 60/F    | Hepatolithiasis      | 1.5 cm/single/left lobe            | Radiofrequency ablation                  | Survive/12 months|
| Zhu et al                | 2012 | 46/F    | Hepatolithiasis      | 5 cm/single/right lobe             | Right hepatectomy                        | Survive/19 months|
| Morito et al             | 2013 | 55/F    | Colon cancer         | 2.6 cm/single/right lobe           | Subsegmentectomy                         | Died/17 months   |
| Wilson et al             | 2013 | 34/M    | Liver foregut cyst   | 10 cm/single/right lobe            | TACE, PVE, resection and chemotherapy    | Survive/6 months |

PVE = portal vein embolization; TACE = transcatheter arterial chemoembolization; TAI = transcatheter artery infusion.
pathological examinations. Secondly, positive staining for cytokeratin (CK) 7, CK8, CK14, CK18, and/or CK56 would indicate basal cells of keratinized squamous epithelium origin of the cancer cell. And positive staining for biliary CK19 would confirm the bile ductal ontogeny of the neoplastic cells. And more importantly, exclusion of possible tumor origin from other organs, such as lungs, thyroid, esophagus, gastrointestinal tract, ENT, etc. is necessary before the diagnosis of primary liver SCC. In our cases, squamous cancer from these possible sites other than liver had been ruled out clinically, radiologically, and/or endoscopically, and then the tumors were diagnosed as primary SCC of the liver.

**Treatments and Prognosis**

The prognosis of primary liver SCC is extremely grave even after extensive procedure to achieve radical resection of the lesions. Among the previous 19 reported cases undergoing surgical resection, 8 cases survived over 12 months and 11 cases died within 1 year. The 1 case in the present study died of tumor recurrence and metastasis 18 months after radical surgery. Among the 13 reported cases undergoing palliative treatments, only 2 of them survived more than 12 months. And the 3 cases in the present study all died within 1 year after the first admission. In the cohort of the present study, patients undergoing radical surgery had longer overall survival time than those undergoing palliative treatment (median survival 17 vs 5 months, P = 0.005). Therefore, complete surgical excision of the tumor is strongly recommended rather than simple drainage, marsupialization, or partial excision.

Systemic or intrahepatoarterial chemotherapy might be useful in some patients with no opportunity for surgery. Kaji et al recommended a protocol of intrahepatoarterial chemotherapy with cis-diaminedichloroplatinum and 5-fluorouracil, which has been used in the treatment of esophageal cancer with liver metastasis. And finally, this patient with primary liver SCC survived for 23 months without surgery. Chemotherapy, TACE, and even radiation could be used in these inoperable patients or as adjuvant treatments before and after surgery.

Another finding in the present study was that patients with bile duct stones seemed to be better in prognosis than those with liver cysts (median survival 18 vs 7 months, P = 0.090). The reason was, however, unclear. It was possible that patients with bile duct stones always presented with more overt symptoms, and received auxiliary examinations and treatments much earlier than those with liver cysts. Also, it is likely that primary liver SCC originating from bile duct stones and liver cysts might be different in etiology, and even clinical course, which needs to be further investigated.

**CONCLUSION**

In summary, primary liver SCC seems to be mostly originated from liver cyst or hepatolithiasis, the causes of carcinogenesis and etiopathogenesis of which, however, need to be further studied. Radical surgery should be firstly recommended, although the prognosis might be unfavorable.

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