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Case report

# Primary squamous cell carcinoma of liver. First case report from Pakistan and South Asia

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ABSTRACT

*Introduction and importance:* Primary squamous cell carcinoma (PSCC) of liver is quite rare and very few cases reported in literature. It has high metastatic rate with poor prognosis. The pathogenesis is unclear, but is generally considered to be correlated with the long-term inflammation or metaplasia of biliary epithelial cells or congenital cyst of the liver. We report here a case of PSCC of liver which mimicked a complex hydatid cyst.

*Case presentation:* A 25 years male admitted with right hypochondrium pain associated with fever and yellowish discoloration of eyes for 20 days. He was jaundiced with epigastric tenderness and deranged liver function tests. When thoroughly investigated with ultrasound, CT abdomen and MRI liver, he was found to have a large cystic lesion in right lobe of the liver. He underwent right hepatectomy, peri-cystectomy of the cyst and T-tube placement in common bile duct. Histopathology of the resected sample showed primary squamous cell carcinoma of liver. Patient was discharged after 7 days and died after 6 months due to acute liver failure.

*Clinical discussion:* Because of a very low incidence of hepatic SCC, there is not a single definite therapeutic regime and various different methods of management include surgical resection, generalized chemotherapy, radiotherapy, Hepatic Arterial ChemoEmbolization (HACE) and the combinations of these therapies.

*Conclusion:* PSCC is a rare condition of the liver and is associated with other benign liver conditions such as non-parasitic and epidermoid cysts. Histopathology with radiological investigations are needed to diagnose and treat this aggressive tumor before it metastasizes.

## 1. Introduction

Generally squamous cell carcinoma is common type of skin cancer which occurs in the squamous cells of the skin which makes the middle and outer layers of the skin [1]. Primary squamous cell carcinoma (PSCC) is a rare primary tumor of the liver. Squamous cell carcinoma (SCC) arises basically due to malignant transformation of the organs which are lined by squamous epithelium. The most common malignancy of the liver is metastasis from different organs of the body the most common of these are from rectum and breast [2]. Squamous epithelium is not found in liver and thus it is very unlikely that primary squamous cell carcinoma can be found in liver. That is the reason only 31 cases of PSCC are reported in literature since 1970.

The exact pathology of developing SCC in liver is still unknown. Many studies correlate the high incidence of PSCC in male gender or association of PHCC with conditions like hepatolithiasis, liver teratoma or chronic cholecystitis [3]. Majority of the authors of previous published case reports are of view that chronic inflammation or bile duct irritation leads to secondary development of squamous metaplasia and in turn transformation of the epithelium [4]. As compared to the SCC of skin which is usually non-threatening, PSCC is a very rare and aggressive tumor with overall survival of less than 12 months [5].

In this case report, we are going to present a case of PSCC in 25-year-old male which was initially diagnosed as case of biliary cystadenocarcinoma/cystadenoma and later after surgical resection histopathology came out to be PSCC. This case is first reported case of PSCC from Pakistan and South Asia as well.

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## 2. Presentation of the case

A 25-year-old male presented to us with a three weeks history of dull, right sided upper abdominal pain, moderate in intensity with no radiation and associated with off and on high grade fever. There was no history of weight loss or anorexia. He was an ex-smoker and tobacco addict with no other co-morbidities. On examination he was jaundiced with otherwise normal general physical examination with no palpable lymph nodes. Abdomen was soft with mild right hypo-chondral and epigastric tenderness with no organomegaly. Respiratory, cardiovascular and Neurological systems were unremarkable. His baseline blood tests on admission including alpha fetoprotein (AFP), C Reactive Protein (CRP), Procalcitonin (PCT|) and hydatid cyst serology were normal except bilirubin (2.3 mg/dL), Alkaline Phosphatase (194 IU/L), Gamma-Glutamyl Transpeptidase (154 IU/L), albumin (2.9 g/dL), Total leukocyte count (15,200/μL) and International normalized ratio (INR) of 1.2. Ultrasound (USG) abdomen showed no evidence of gall stones. Liver was enlarged with increased echogenicity and a cystic lesion of about 9.0 × 8.6 cm in right lobe of liver with internal echoes. It appeared irregular and heterogeneous with solid and cystic areas giving the possibility of liver abscess. Contrast Enhanced Computer Tomography (CECT) of Chest, Abdomen and Pelvis (CAP) confirmed a large multi-locular, multi septate cystic lesion in seg IV, V, VI and VII having communication with intrahepatic biliary ducts and small solid enhancing component with possibility of biliary cystadenoma (Fig. 1). Lungs and skeleton were clear of any metastatic lesions.

This patient was discussed in weekly hospital Multi-Disciplinary Team (MDT) meeting in which plan of further investigating the lesion was made with Magnetic Resonance Imaging (MRI) of liver. MRI of liver showed a large (12 × 10 × 10.2 cm) multilocular cystic lesion in right segments VIII, VII, V & IVa of liver with soft tissue component and biliary communication with right and left hepatic ducts. Right and left intra-hepatic ducts were mildly dilated (Fig. 2). Common bile duct (CBD) was of normal caliber. Imaging features favors biliary cystadenocarcinoma/cystadenoma. Plan of surgical excision of the lesion was made.

After informed and written consent from patient for surgery under general anesthesia, Patient underwent right hepatectomy, pericystectomy of the cyst. During surgery there was a large infected, ruptured cyst in right lobe of liver with thick pus, pus in right para-colic gutter and Intra-cystic biliary communications. Cholecystectomy was done and intraoperative cholangiogram was done which showed communication of the cyst cavity with biliary system. Hilar dissection was done and right hepatic duct, right portal vein and right hepatic artery was ligated. Portal plate was then divided and left hepatic duct was anastomosed with CBD and T-tube was passed in CBD. The resected part of liver was sent for histopathology. Postoperative course was complicated by right sub-phrenic collection for which ultrasound guided Percutaneous transhepatic catheter (PTC) was inserted. Patient was discharged on 7th post operation day with T-tube & PTC tube in situ and advised follow-up on weekly basis for one month. Patient was given 10 days of broad-spectrum intravenous antibiotics post operatively along with intravenous antifungals. PTC tube was removed on first follow-up after two weeks.

Histopathology of the resected lesion showed a poorly differentiated squamous cell cancer arising from a cystic lining, lined by stratified squamous epithelium arranged in nests of atypical squamous cells. Individual tumor cells were large, pleomorphic, hyperchromatic and with high nuclear to cytoplasmic ratio, also showing keratin Perl formation (Fig. 3). Peri neural and vascular invasion was present. P63-Positive & P16-were positive. R0 resection was confirmed by histological findings.

Patient was again discussed in Hospital MDT and after reviewing the histology report, plan of Positron Emission Tomography (PET) CT was made to rule out any other lesion in the body but patient remained non complaint to follow-up and unfortunately presented in the emergency department 6 months after discharge with sign and symptoms of acute liver failure and despite active resuscitation patient ultimately died.

## 3. Discussion

Since 1970 till date, only 31 cases of PSCC are available in literature. In these reported cases the age group in which patients presented is not fixed as review of literature showed that the minimum age of patient presenting with PSCC is 18 years while the maximum age reported is 82 years [6]. The age of patient in this case report is 25 years and in literature only 3 patients are reported below age of 25 years, 2 were 21 years old and one was 18 years old. This showed that PSCC can occur at any age group and this rare tumor is not confined to any age group.

Among available reported cases of PSCC, majority of the patients presented with nonspecific symptoms of abdominal pain with or without jaundice. Majority of the presented patients were diagnosed as cases of liver cysts on imaging [7]. Among 31 reported cases, 19 (61.3) cases presented with liver cysts in which the origin of development of liver cyst is unknown. Other liver conditions which were later found to be SCC of liver included hepatolithiasis and gall stone disease. The patient presented in this case report also presented with vague right upper quadrant pain with jaundice and on CECT CAP it was found to have liver cyst. There were no co morbid conditions in this patient and no positive family and past medical or surgical history. Thus, the pathogenesis of PSCC is still not clear and it is proposed that the origin of pathogenesis is PSCC is continuous irritation or inflammation of biliary duct epithelium due to any cause like hepatitis or cholangitis. Liver cyst may cause squamous metaplasia of the biliary epithelium leading to malignant transformation. This theory is supported by the fact that majority of the cases of PSCC had liver cysts or hepatolithiasis [8].

Still the diagnosis of PSCC is the diagnosis of exclusion as metastatic

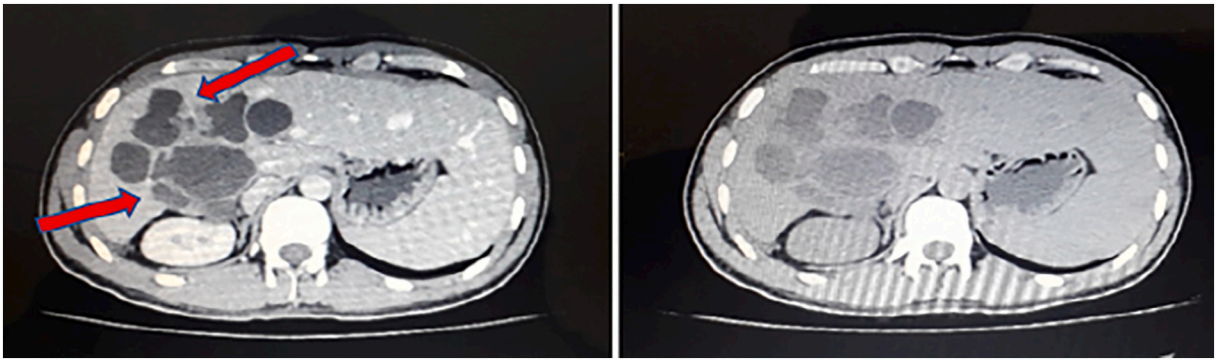

**Fig. 1.** CECT CAP confirmed a large multi-locular, multi septate cystic lesions (red arrows) having communication with intrahepatic biliary ducts and small solid enhancing component. Possibility of biliary cystadenoma. No metastatic lesions. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

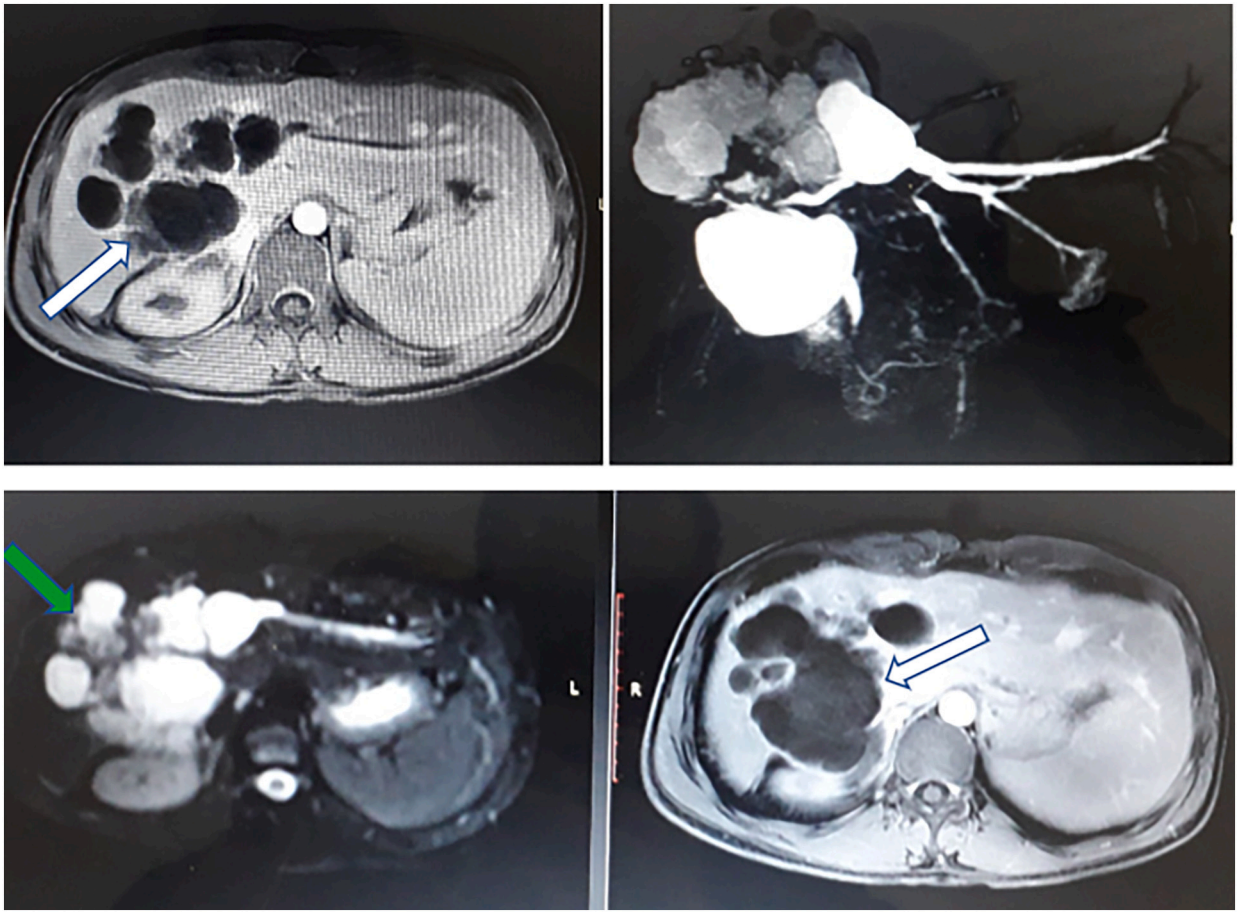


**Fig. 2.** MRI with contrast of liver showed a large 12 × 10 × 10.2 cm, multilocular cystic lesion in right segments VIII, VII, V & IVa of liver (white arrow) with soft tissue component and biliary communication with right and left hepatic ducts Right and left intra-hepatic ducts were mildly dilated (green arrow). CBD was of normal caliber. Imaging features favor biliary cystadenocarcinoma/cystadenoma. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

SCC is present in majority of the cases in liver. So before making the diagnosis of PSCC, all those areas of the body from where SCC can metastasize to liver should be assessed in detail like skin, head and neck and lungs [7]. Our patient had no medical and family past history of such disease and the only symptom he experienced was pain upper abdomen first which was followed by jaundice. In most of the cases Alanine transaminase (ALT) and aspartate aminotransferase (AST) and bilirubin were found elevated which suggest chronic inflammation of the liver epithelial cells [9]. But in our case ALT and AST were in normal range while bilirubin was elevated (2.3 mg/dL). Also, AFP, CA19-9 and Gamma glutamyl transferase were also in normal range.

CECT CAP is considered as important preoperative imaging modality in liver disease. Intrahepatic bile duct stones, intrahepatic biliary dilatations and hepatic cysts can be clearly ruled out on CECT. MRI is of importance to evaluate the biliary anatomy and communication of liver cyst with bile ducts [10]. Preoperative liver biopsy can further confirm the diagnosis but it is not routinely done in patients with liver cysts. Immuno-histological staining is usually positive for p63, p16 CK5/6 as reported in literature [11]. The biopsy of our patient was positive for p63 and p16.

There is no standard treatment protocol for PSCC liver. But radical surgery including excision of the cyst, if possible, remains the mainstay of treatment as it increases the life expectancy from 5 months with palliative treatment to 17 months [12]. Surgical resection is preferred over drainage or partial resection of the cyst in terms of recurrence of disease. If surgery is not possible then systemic intraperitoneal chemotherapy with cisplatin and 5FU is recommended [4]. In comparison with patients with bile duct stones, patients having liver cysts have poor prognosis. According to available literature 12 (37.5 %) patients survived out of 31 [2].

## 4. Conclusion

Primary SCC of the liver is a very rare cancer so this diagnosis is often out of mind of surgeons when they are dealing with any kind of hepatic cyst/tumor. Because of its association with other benign lesions of the liver, its diagnosis is usually delayed. Its diagnosis requires a detailed thorough investigation along with histo-pathological evaluation preoperatively in order to diagnose and manage the cancer surgically followed by chemo or radiotherapy, before it metastasizes.

## Author contribution

Muhammad Atiq: study concept or design, data collection.

Ahmed Siddique Ammar: data analysis or interpretation, writing the paper.

Rabiaa Mehmood Ali: study concept or design, data collection.

Siraj Haider: data analysis or interpretation, writing the paper.

Imran Ahmed: data analysis or interpretation, writing the paper.

Faisal Saud Dar: study concept or design, data collection, data analysis or interpretation, writing the paper.

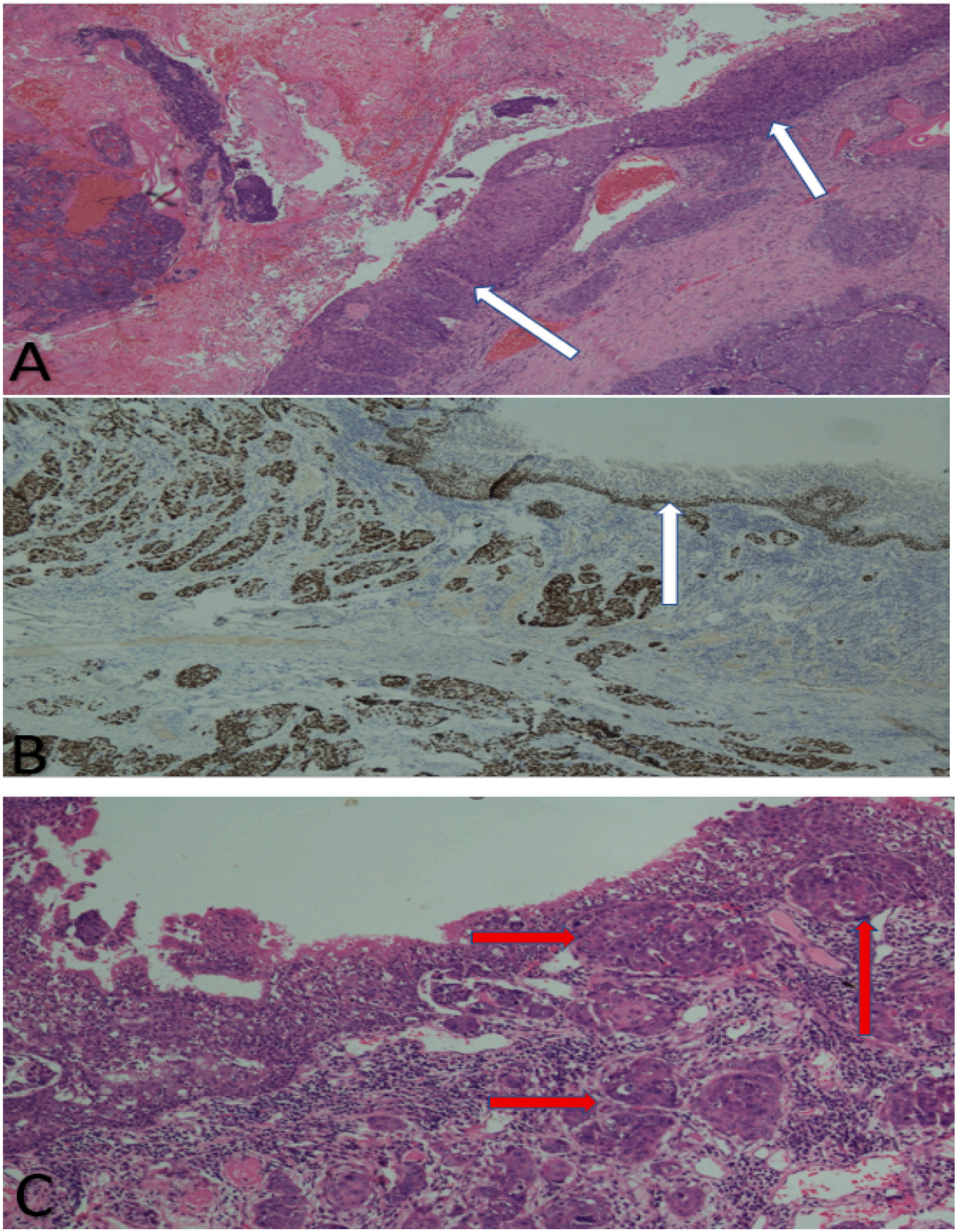


**Fig. 3.** (A & B) showing poorly differentiated squamous cell cancer arising from a cystic lining, lined by stratified squamous epithelium arranged in nests of atypical squamous cells (White arrows). C showing Individual tumor cells were large, pleomorphic, hyperchromatic and with high nuclear to cytoplasmic ratio, also showing keratin Perl formation.

## Registration of research studies

None.

## Guarantor

Ahmed Siddique Ammar.

## Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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## Ethical approval

The study is exempted from ethical approval in our institution.

## Declaration of competing interest

None.

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