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Single Case

Spontaneous Rupture of Hepatocellular Carcinoma in a Young Patient with Fatal Outcome

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Keywords
Bleeding hepatocellular carcinoma · Ruptured hepatocellular carcinoma · Spontaneous liver rupture · Case report

Abstract
Spontaneous rupture of hepatocellular carcinoma (HCC) is a potentially life-threatening complication. Diagnosis may be difficult, particularly in the absence of known liver cirrhosis or tumor. A 20-year-old male patient presented with progressive abdominal pain and shock. His past medical history was uneventful. Anemia, acute renal failure, and abnormal liver function test were demonstrated. Mild hepatomegaly, perihepatic and flank fluid, and multiple hypodense liver lesions suggestive of intrahepatic metastases or multifocal HCC were revealed by computed tomography. Two actively bleeding liver tumors and multiple tumors in a noncirrhotic liver were found. Hemostatic suture and perihepatic packing were performed. The patient remained in critical condition, with a fatal outcome 48 h later. Histopathologic analysis reported HCC and absence of cirrhotic changes. HCC spontaneous rupture incidence is reported between 2.3 and 26%. Median age is 65 years. No liver cirrhosis is found in one-third of patients, with a median age of 51 years. Sudden onset of abdominal pain and shock is observed in the majority of cases. An accurate preoperative diagnosis improves to 75%

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with ultrasound and computed tomography. Besides hemodynamic stabilization, there is no general agreement on the best treatment option. Transarterial embolization, surgical perihepatic packing, suture plication, and hepatic artery ligation are useful methods of hemostasis in unstable patients. Mortality has been reported from 16.5 to 100%. The histopathologic finding of HCC in a noncirrhotic liver represents a less frequent presentation. A case of spontaneous rupture of HCC carcinoma and a noncirrhotic liver in a young patient is herein reported.

Introduction

Hepatocellular carcinoma (HCC) is the most common primary hepatic malignancy. It represents the sixth most common malignancy, and the third leading oncologic cause of death worldwide. The high incidence of chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections contribute to the increased incidence [1]. Spontaneous rupture of HCC is a potentially life-threatening complication and occurs with variable geographic incidences between 2.3 and 26%. Ruptured HCC is associated with a mortality rate of 25–100% [2]. Abdominal pain and hemodynamic instability constitute the most common clinical presentation. Diagnosis of ruptured HCC may be difficult, particularly in patients with no history of liver cirrhosis, liver tumor, or HBV or HCV infection and due to hemodynamic instability [3, 4]. A case of spontaneous rupture of HCC and a noncirrhotic liver in a young patient with no history of HBV or HCV infection is herein reported.

Case Report

A 20-year-old male patient presented to the Emergency Department of our hospital with progressive abdominal pain and dyspnea during the previous 10 days, followed by cyanosis during the previous 3 days. His past medical history was uneventful. He denied alcohol intake, drug use, and transfusions. At admission, physical examination revealed a heart rate of 112 beats per minute, a blood pressure of 80/50 mm Hg, a respiratory rate of 22 breaths per minute, and a temperature of 36°C. The patient was icteric and showed central cyanosis. His abdomen was distended, and bowel sounds were hypoactive, with generalized tenderness, guarding, and rebound tenderness. Liver and spleen were not palpable. Blood count showed hemoglobin of 10.9 g/dL, a platelet count of 184 × 10^9, and a white cell count of 19.2 × 10^9, with predominance of neutrophils (84.9%). Coagulation screening tests showed a prothrombin time of 30.5 seconds, activated partial thromboplastin time of 37.1 seconds, and international normalized ratio of 2.77. Biochemical analysis showed a blood glucose of 69 mg/dL, serum creatinine of 2.45 mg/dL, blood urea nitrogen test 81.6, sodium 127 mmol/L, potassium 5.19 mmol/L, chloride 89 mmol/L, calcium 4.25 mmol/L, and phosphorus 3.8 mmol/L. Liver functions showed total bilirubin and direct bilirubin levels were 5.18 mg/dL and 3.47 mg/dL, respectively. Total protein was 6.44 mg/dL, serum albumin 3.24 mg/dL, serum alanine aminotransferase 573 U/L, serum aspartate aminotransferase 1,256 U/L, serum alkaline phosphatase value 456 U/L, and serum lactic dehydrogenase 6,744 U/L, and arterial blood gas analysis showed pH 7.29 and lactate 8.2 mmol/L. The patient initially received crystalloids, followed by packed red blood cells and fresh frozen plasma. Abdominal computed tomographic (CT) scan showed mild hepatomegaly, perihepatic and flank fluid, and multiple hypodense liver lesions suggestive of intrahepatic metastases or multifocal HCC

(Fig. 1). Transcatheter arterial embolization (TAE) was unavailable at the time of presentation. At emergency laparotomy, 2,800 mL of blood in the abdominal cavity were discovered; two actively bleeding liver tumors in segments III and VI, and multiple small nonbleeding tumors were observed (Fig. 2). The liver did not show a cirrhotic aspect, and biopsy was taken. Suture plication and surgical perihepatic packing were performed. The patient was admitted to the Intensive Care Unit, under mechanical ventilatory support, with hemodynamic instability and coagulopathy. Despite the proper management, the patient had a fatal outcome 48 h after the surgical procedure. Histopathologic analysis reported HCC and absence of cirrhotic changes (Fig. 3).

Discussion

HCC is the most common primary liver malignancy. It represents the sixth most common cancer worldwide and the third leading cause of death secondary to cancer. Chronic HBV infection is the world's leading cause of HCC, while chronic HCV infection is the main cause in Southern Europe and North America. Although 70–90% of patients with chronic hepatitis B who develop HCC will have cirrhosis, it may be present without cirrhotic changes. Cirrhosis secondary to chronic HCV infection, alcoholic liver disease, and nonalcoholic steatohepatitis, among others, are also important contributing factors [1].

Spontaneous rupture of HCC with intraperitoneal hemorrhage is a potentially life-threatening complication. HCC is responsible for 15% of cases of spontaneous hepatic hemorrhage in areas of high prevalence of this tumor, whereas in areas of low prevalence, it represents the second cause, only after hepatic adenoma [5].

In Asian countries, a 2.3–26% incidence of spontaneous rupture of HCC has been reported, while in Western countries, it has been observed in less than 3% of HCC patients [2, 6]. Aoki et al. [6] identified 1,160 patients with spontaneous ruptured tumor from a nationwide database of 49,708 HCC cases, representing 2.3%.

In a study from London, the median age of patients with spontaneous ruptured HCC was 65 years. No liver cirrhosis was found in one-third of patients, in whom the median age was 51 years [3].

The mechanism that leads to spontaneous tumor rupture is still not completely understood. Factors such as tumor dimensions, subcapsular location, tumor necrosis, local increase in tumor pressure, vessel erosion, portal hypertension, coagulopathy, and previous vascular injury might contribute to HCC rupture [4]. Battula et al. [3] reported a mean tumor size of 8.5 cm (range 3–13) and multifocal HCC in 42.8% of their patients. Free intraperitoneal bleeding is most commonly caused when the HCC is peripherally located, with no surrounding liver parenchyma [7].

The most common clinical presentation is characterized by abdominal pain, hemodynamic instability, and peritoneal irritation [7]. A sudden onset of abdominal pain is considered the most common symptom of ruptured HCC and has been reported in 66–100% of patients. Shock has been reported in 33–90% of cases [2, 4]. When the HCC is in a more central location and is not proximal to the liver capsule, peritoneal irritation due to bleeding may not be evident [7]. Abdominal pain has been found to be the only independent factor predicting ruptured HCC. Lower hemoglobin concentration level (less than 10 g/dL) has also been associated with ruptured HCC [8].

Diagnosis of ruptured HCC may be difficult, particularly in patients with no history of liver cirrhosis, liver tumor, or HBV or HCV infection and due to hemodynamic instability.

Diagnosis may be made until emergency surgical exploration [3, 4]. While preoperative diagnosis of ruptured HCC has been reported in only 25% of patients, diagnostic accuracy has improved with ultrasound, CT, and celiac angiography with confirmation in the range of 66–75% of cases [2, 9]. CT is a reliable technique for HCC detection, determination of number, size and location of tumors, and presence of bleeding and hemoperitoneum. The site of active bleeding can hardly be demonstrated. Extravasation of contrast material from the tumor can be demonstrated by a hepatic angiography in 13.2–35.7% [2].

Initial management of acute hemorrhage in ruptured HCC requires hemodynamic stabilization, blood transfusion, and coagulopathy correction, followed by surgical, cardiopulmonary, and liver function evaluation. The primary goal is hemostasis. Liver functional status and stage of the HCC must be considered [2, 5]. Hemodynamic stabilization, blood transfusion, and coagulopathy correction may result in bleeding control. In a study by Leung et al. [10], no further hemostatic treatment was required in 47.3% of patients.

TAE is the best method to achieve hemostasis in patients with hemorrhage secondary to ruptured HCC, particularly in hemodynamically unstable patients [5]. Hepatic angiography is performed via a femoral approach with selective catheter insertion in the hepatic artery supplying the bleeding tumor. Sterile absorbable gelatin sponges, stainless steel coils, and polyvinyl alcohol sponges have been used to achieve arterial occlusion. Gelatin sponges may be preferred over coils in order to facilitate further transarterial chemoembolization [11]. Success rate has been reported in ranges of 53–100% with in-hospital mortality rates of 0–55.5%, due to recurrent bleeding and liver failure [2]. TAE may not be possible in up to 20% of patients. Main portal vein thrombosis, arteriovenous shunting, and technical failure may limit the procedure feasibility [12].

Emergency surgical procedures are indicated when bleeding persists after TAE or this procedure is not feasible, and in hemodynamically unstable patients where diagnosis is made at laparotomy [2, 5]. Hepatic resection is among the best treatment strategies for ruptured HCC but it can be particularly demanding in hemodynamically unstable or advanced cirrhotic patients. The in-hospital mortality rates have been reported in the range of 16.5–100%. Surgical perihepatic packing, suture plication, and hepatic artery ligation have been reported as useful methods for hemostasis in unstable patients [2].

Liver failure may complicate the acute phase in 12–42% of patients with ruptured HCC, leading to in-hospital mortality rates of 25–100% [2]. Chen et al. [13] reported a review of 15 studies including 835 patients with ruptured HCC, where 30-day mortalities of 71, 50, and 38% were observed among patients treated by conservative treatment, emergency surgical procedures, and TAE, respectively. Emergency surgical procedures included resection, suture plication, perihepatic packing, or hepatic artery ligation.

There are no randomized trials to determine the best method of hemostasis and there is no general agreement about the best treatment option for ruptured HCC. In a systematic review by Lai and Lau [4], TAE showed a high success rate for hemostasis during the acute phase (53–100%), with a lower 30-day mortality rate compared to surgical approach (0–37% vs. 28–75%). For definitive treatment, staged liver resection showed a higher resection rate and a lower in-hospital mortality rate than single-stage emergency liver resection.

In a retrospective multicenter European study by Schwarz et al. [14], hemostasis was achieved by interventional hemostasis, emergency liver resection, and conservative medical management in 62, 18, and 15% of patients, respectively. Best supportive care was chosen for 7 (5%) patients. Bleeding recurrence was observed in 22% with resultant mortality in 52%. The global mortality rate was 24%.

Serum bilirubin level, shock on hospital admission, and prerupture disease state are important predictors of survival in the acute phase [4]. In a study by Tan et al. [15], shock on admission and higher blood transfusion requirement were significant independent factors affecting mortality. Poor liver reserve, advanced disease, and severity of hemorrhage were associated with poor prognosis. Schwarz et al. [14] reported that a bilirubin level >17 μmol/L, bleeding recurrence, and ICU admission after initial management were associated with in-hospital mortality.

The case herein reported of spontaneous ruptured HCC represents an unusually young patient compared to the Western presentation age [3]. The absence of abdominal trauma or risk factors such as chronic HBV or HCV infection, alcoholic liver disease, nonalcoholic steatohepatitis, or liver cirrhosis made the liver a less probable source of bleeding. Clinical presentation of progressive abdominal pain and shock in an anemic patient prompted the evaluation for a potential bleeding. Jaundice and abnormal liver function tests were indicative of hepatic disease. CT findings and the unavailability of TAE urged for laparotomy where major bleeding from multifocal liver disease was demonstrated. A late medical consultation, organ failure secondary to a progressive bleeding, and the hemorrhage magnitude contributed to the fatal outcome. The histopathologic finding of HCC in a noncirrhotic liver represents a less frequent presentation.

A rare case of spontaneous rupture of HCC carcinoma and a noncirrhotic liver in a young patient is herein reported.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

David F. Pinal-García (author), Carlos M. Nuño-Guzmán, Audrey Gómez-Abarca, Jorge L. Corona, and Ismael Espejo (co-authors) have no conflicts of interest, sponsorship, or funding arrangements to declare.

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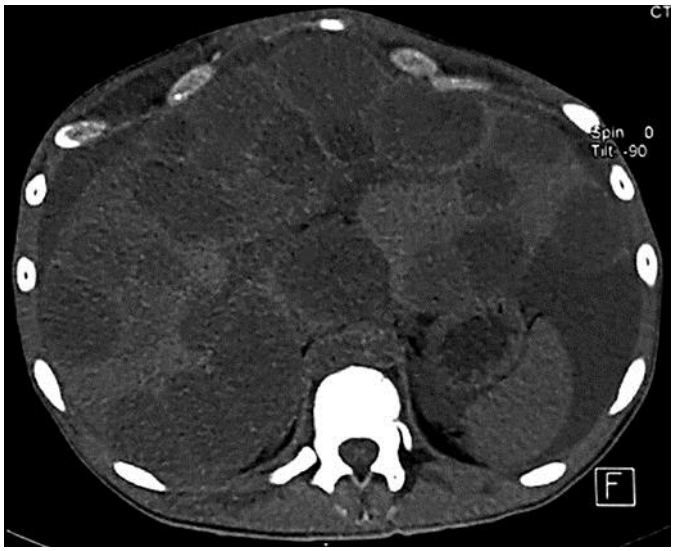

Fig. 1. Noncontrast CT revealed mild liver enlargement, and 2–8 cm round-shaped lesions with regular contour and central hypodensity, disseminated throughout the liver, are observed. This is suggestive of intrahepatic metastases or multifocal HCC.

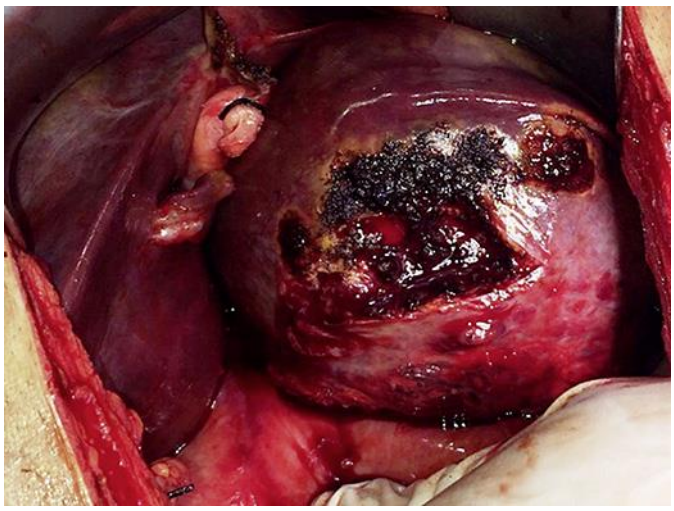

Fig. 2. Surgical aspect of one of the two actively bleeding liver tumors.

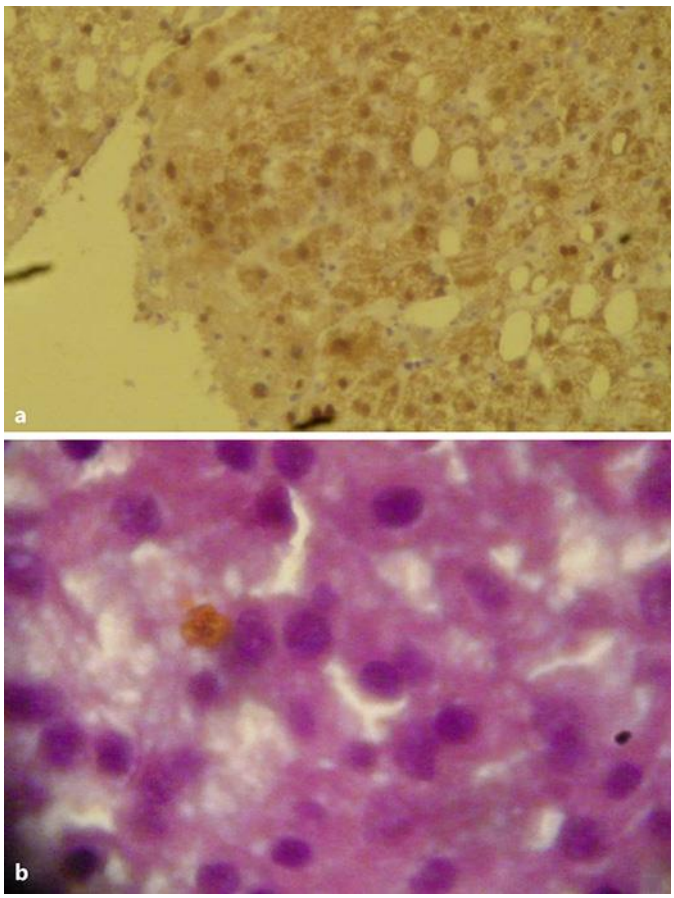

Fig. 3. **a** Histologic examination showed acidophilic and polygonal neoplastic cells, with a solid pattern and bile pigment formation in an intracytoplasmic cumulus. Histologic elements are suggestive of HCC. Hematoxylin and eosin stain, ×40. **b** Immunohistochemical analysis revealed intracytoplasmic positive reactivity for alpha-fetoprotein in neoplastic liver cells. Immunoperoxidase stain, ×10.