

SPONTANEOUS RUPTURE OF HEPATOCELLULAR CARCINOMA AND HEMOPERITONEUM-MANAGEMENT AND LONG TERM SURVIVAL

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ABSTRACT

Aims: Complications of HCC as spontaneous rupture and hemoperitoneum are life threatening and have been observed particularly in patients with superficially dislodged tumors with associated cirrhosis.

Methods: Retrospective analysis of patients from hepatobiliary and liver transplantation units. Three cases for the past 15 years were found.

Results: Of all three patients with ruptured HCC, one was operated in emergency because of positive abdominal puncture for hemoperitoneum and active bleeding. In the other two patients, after emergency diagnostic US, CT and angiographic study, it was decided to perform selective embolization to stop bleeding and stabilize hemodynamic and in second stage proposed liver resection. The age of the patients at time of first accident was 36, 58 and 75, respectively two men and a woman. All patients were diagnosed with associated liver disease-cirrhosis.

Diagnostic procedures and pathologic specimens showed superficially localization of ruptured tumoral nodules: predominantly in right liver lobe. The number of lesion was between 1 and 3, and in later stage, after progressing of the cancer process, it was diagnosed multiple.

The mean size of tumor nodule was 3.0 cm. Three times repeated rupture was treated none surgically by chemoembolization.

The 3, 5 and 10 year survival was 100%.

Key words: hepatocellular carcinoma; spontaneous rupture; long-term management

INTRODUCTION

Hepatocellular carcinoma (HCC) can be present with various clinical signs depending on the associated liver disease, location and patient activity. Spontaneous superficial tumor rupture and active bleeding are the most life threatening situations requiring emergency diagnosis and therapy.

Frequency - it is uncommon and potentially fatal

condition with a reported incidence of 2.9% -26% of patients with HCC (1, 2). A high incidence of spontaneous rupture and hemoperitoneum has been reported in Asia: 26% in Thailand (3), 14.5% in Hong-Kong (4). In Europe and America incidence is relatively low between 2% and 7% of all cases with HCC (5).

Mechanism- many authors believe that disruption of friable artery or tier in the surface of a tumor under high pressure could cause rupture. Minimal trauma or normal respiratory movement may cause superficial laceration and bleeding. It is important for tumors situated under the right diaphragm (6).

The vascular injury was presented more frequently in the patients with ruptured HCC rather than in the patients with nonruptured HCC. Vascular injury included elastin proliferation, collagenase expression and collagen fibril degradation. During the process of vascular injury, vascular permeability was increased, and inflammation cells could emigrate into vascular wall to release proteinase and damage the elastin fibril. Due to the growth factors released with the vascular injury, smooth muscle cells were stimulated to synthesize collagenase and digest the collagen fibril (7) and to synthesize a large number of elastin. In patients with ruptured HCC, the proliferation of elastin was found where elastase was absent around the blood vessel, and was absent where expression of elastase was positive (8).

Based on the vascular injury, vascular split could also occur in small tumor with a lower incidence so far. After the vascular split, intratumoral pressure increased with the formation of hematoma and at the end lead to the tumor rupture and hemoperitoneum.

Clinic- Spontaneous rupture of HCC is a life-threatening condition and patients present with abdominal pain with irradiation to right shoulder, hypovolemic shock and abdominal distention. The diagnosis is confirmed by the presence of hemoperitoneum on abdominal paracentesis. US, CT and arterial angiography have shown lesion and extravasations.

Mortality- previous publications reported high rate

of approx. 85% for conservatively treated patients, and low rate of 64% after surgical procedure such as packing, suturing, electric cauterization and hepatic artery ligation (6).

Now, with selection of every case and used method, and time for procedure, mortality is 0%-2%.

PATIENTS AND METHODS

For the last fifteen years, between 1993 and 2008, by using retrospective analysis, we found three cases with spontaneous rupture of HCC. From the time of diagnosis, treatment, and follow-up we found that for every patient depending on their status, conservative or surgical treatment may help and extend survival. A 10 year survival is 100%.

Case Outlines

Case 1

In 1993 a 58 year old man with a history of alcohol abuse was admitted in the emergency room with acute pain localized in right hypochondria, irradiated to right shoulder and hypovolemia. On examination he was pale, with a tense and distended abdomen and blood pressure 100/60mm Hg. Heart rate 92 bpm. Laboratory was found HCT 0.30, Hb - 94 mg., PT 84%.

For diagnosis were performed standard US, CT and arterial angiography. To confirm intraabdominal bleeding diagnostic paracentesis revealed free peritoneal fluid.

Imaging, especially angiography presented tumoral mass with 3cm in diameter localized in segment VII-VIII with active extravasation intraabdominally. Followed arterioembolization helped to stabilize hemodynamic and after second chemoembolization, four months later, active surgical resection: wedge liver resection of segments VII-VIII was proposed

After seven years clear follow-up period, in 2000 multiple implants were found intraabdominally, three with 10 cm in diameter. Surgical intervention for resection and clearness was proposed

In 2002, nine year after first rupture of HCC, routine US and CT confirmed new 5 cm nodule at segment IV. Chemoembolization was method of choice.

Survival was 11 years and 3 months.

Case 2

In April 1997, at department of emergency was admitted 36 year old African man with a previous anamnesis for cirrhosis and positive antibody for HBV, clinical signs of abrupt pain in right hypochondria and unstable hemodynamic.

Proposed abdominal US, CT and arteriography confirmed single 8 cm tumor mass located in segment II-III, superficially without active bleeding and extravasations of contrast.

Patient's status permitted liver resection - left hepatectomy. Discharged in 8 postoperative days with 4-6

months period of follow-up.

In 2007, after ten years clear interval, he presented for second time spontaneous rupture and Child-Pugh B liver status. CT confirmed three tumoral lesions in segment VI-VII with diameters of 2, 5 cm and IVC. Conservative treatment with chemoembolization was having good results.

The same patient for a period of 10 years and 9 months presented the 3rd and 4th time HCC spontaneous rupture with non significant hemodynamic dysfunctions.

Because of multiples lesions, chemoembolization was the best decision for therapy.

At time of presentation of this article patient is alive: 11 years and 3 months.

Case 3

A 75- years-old woman with previous history of HBV and cirrhosis, presented in February 1999 to emergency room with pain in right hypochondria and irradiation to right shoulder, abdominal distention, hypovolemic shock, irregular heart beating and low blood pressure - 110/75 mmHg. After hemodynamic resuscitation, she was submitted to diagnostic US, which revealed a large amount of intrabdominal fluid. Arterial angiography showed two hypervascularized subcapsular formations in 3.5 cm of diameter in right liver lobe (segments V-VI) with active extravasation of injected contrast.

Selective embolization helped to stop the bleeding and after period of eight days patient obtained wedge resection of segments V-VI.

Intrabdominal cytology was positive for tumoral cells.

Active follow-up confirmed after clear time of five years two new lesions in segment VII, treated with chemoembolization.

In October 2006 the patient presented with second spontaneous rupture and diagnostic imaging showed nodule in left lobe.

The chemoembolization is choice for conservative life supporting treatment.

Survival is 10 years and 2 months.

RESULTS:

Despite the number of patients (only three), we observe good results after treatment of spontaneously ruptured HCC.

No difference between man and woman or different age groups.

For appearance, associated liver disease is diagnosed. Historically, in all three patients cirrhosis was found.

Main clinical signs, as abdominal wall distention, abrupt pain localized in right hypochondria and irradiated to right shoulder were observed in patients' presentation at emergency unit.

Tumor location was predominantly in the right hepatic lobe and multiple nodules were found (mean 2, range 1-4).

The mean size was 3.5 cm; the smallest was 2.5 cm and the biggest 8 cm.

Diagnostic algorithm includes:

- Hemodynamic evaluation
- US, CT, Angiography with followed by selective arterial embolization (Fig. 1)
- Intraabdominal paracentesis

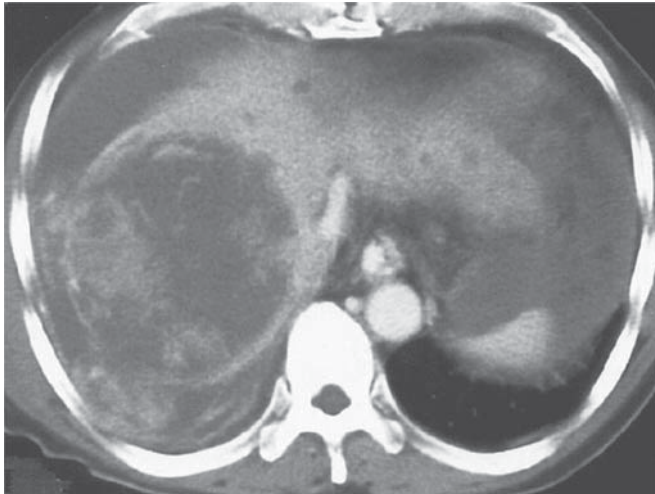


Fig1. CT of HCC of right lobe with spontaneous rupture

The treatment depended on the patient's condition:

- Immediate treatment was performed in two patients- selective arterial embolization for stabilizing of hemodynamic and in period of 8-30 days second stage – liver resection.
- In one patient with active bleeding and lesion localized in left lobe, method of choice was one stage left hepatectomy.

Repeated spontaneous rupture was observed in two patients. We found aggravation of associated liver disease for period of 6 years which compromised liver function parameters and architecture. Minimal trauma factors may cause rupture.

Chemoembolization is method of choice for continuous therapy.

Intraabdominal dissemination was present in all patients, but clinical significance of metastasis was observed in one: compression and bowel obstruction masses necessitated laparotomy and resection.

A 3, 5 and 10 years survival is 100%.

DISCUSSION

Spontaneous rupture of HCC is a life threatening condition and emergency diagnosis and hemodynamic resuscitation may save the patient. Massive intraabdominal bleeding has been the most dangerous complications. It is associated in 98% with previous liver disease, particularly cirrhosis or liver malignancy. The patient usually is

presented with sever abdominal pain with irradiating to right shoulder, and massive hemoperitoneum cause for hemodynamic dysfunction (9). Although CT and angiography can help to identify the source of intra-abdominal bleeding.

It is believed that a tear in the tumor surface or rupture of a feeding artery causes HCC rupture and is resulting in hemoperitoneum (10). The larger protruding tumors might tear more easily and are at the most risk of rupture. Tumors of the left lobe may protrude outward more easily than those of right lobe because of anatomical situation.

Oug et al. (11) consider that small tumors are supplied by the hepatic artery and drained by the portal vein. As a consequence, obstruction of the main branches of the portal vein and portal hypertension are believed to produce a tamponade effect, with subsequent tumor rupture.

Various CT findings of usual manifestations of ruptured HCC can be presented.

HCC rupture usually accompanies hemoperitoneum (12). Moreover, highest-attenuating hematomas are usually closest to sources of bleeding on CT scans, whereas lower –attenuating unclotted blood tends to be located further from bleeding sites.

Active extravasation of contrast material can be differentiated from clotted blood, as the CT attenuation values of extravasated contrast material are indicative of the presence of intravenous contrast material in blood, and thus are significantly higher than those of clotted blood. A finding of contrast material extravasation in HCC represents active bleeding from a ruptured HCC, necessitating immediate treatment, such as, chemoembolization or operation.

HCCs often grow expansively, especially when tumors have an encompassing fibrous capsule (10). In such cases, intratumoral pressure may be elevated, thus predisposing rupture. Multiplanar reformation images using multi-detector row CT can provide improved confidence of contour protrusion of HCC with rupture. Discontinuity or disruption of the hepatic surface neighboring or contacting a HCC is a primary CT finding in the ruptured HCC (13). Discontinuity of the hepatic surface is presumably due to HCC rupture through the hepatic capsule.

Unusual manifestations of ruptured HCCs may be observed as a sudden onset epigastric or right hypochondrial pain due to acute distention of the Glisson capsule. A wide spectrum of imaging findings of ruptured HCC may be encountered, ranging from intra-hepatic tumor rupture to rupture through the hepatic capsule into the peritoneal space.

Management

A treatment of spontaneous rupture HCC was dependent on preruptured disease state, liver function, and severity of bleeding. The two-stage therapeutic approach

to manage ruptured HCC consisted of initial management by conservative method, hemostasis by transarterial embolization(TAE) or surgical means, followed by second-stage hepatic resection or transarterial oily chemoembolization (TACE).

The results of treatment of ruptured HCC could be divided into results of immediate treatment of ruptured tumor and long-term results of definitive treatment of the tumors of patients who survived the initial insult of ruptured HCC. In clinical practice we use the algorithm (Fig.2)

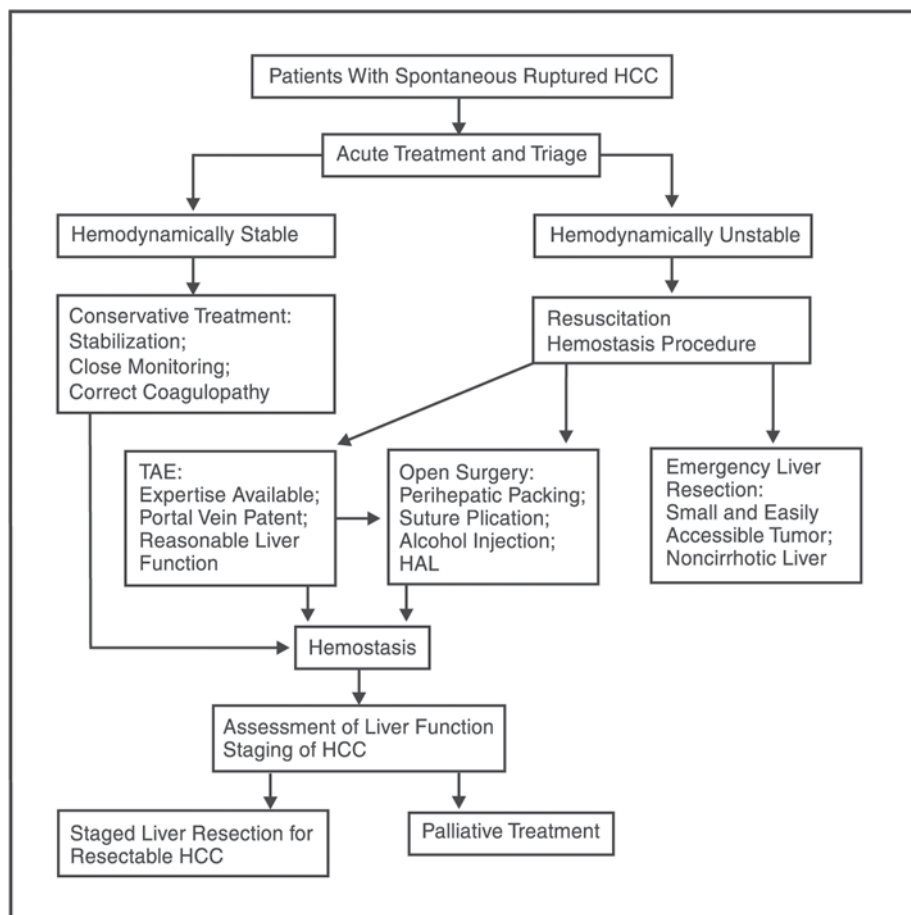


Fig. 2 Algorithm for diagnosis and treatment of spontaneous rupture of HCC

a/ Immediate treatment of ruptured HCC- included conservative management, TAE, laparotomy and surgical hemostasis. Conservative treatment is recommended for patients with stable hemodynamic at initial presentation.

TAE is the first choice of treatment for unstable patients with continuous intra-abdominal hemorrhage. In more than 90% this procedure is successful. It can be unsuccessful, if main portal vein thrombosis is presented and marked arteriovenous shunting occurs in arteriogram.

Laparotomy as conservative treatment includes:

- Laparotomy only
- Ligation of hepatic artery (common hepatic artery, Right or Left hepatic artery)
- Suturing of bleeding tumor
- Perihepatic packing
- Resection or debridement of ruptured tumor

In multivariate analysis, the four independent factors,

evident on presentation, that significantly affected the 30-day mortality of the patients, are:

- (1) Shock on admission
- (2) Hemoglobin levels
- (3) Serum total bilirubin level
- (4) Known diagnosis of HCC before rupture of the tumor

b/ Definitive treatment of HCC- after recovery from the initial stress of ruptured HCC and complete clinical evaluation, the patients are considered for curative hepatic resection. Special care is required during hepatic resection for HCC that has previously ruptured, because injudicious mobilization of the tumor may result in rerupture and bleeding. In case, in which difficult mobilization of the tumor is encountered or when there is a risk of disturbing hematoma at the right subphrenic space, anterior approach hepatic resection is preferred.

c/ Management of patients with multiple implanted intraperitoneal metastases after resection of ruptured HCC

Elevated AFP levels and capsule invasion by tumor cells may predispose posthepatectomy patients to peritoneal implantation from their HCC.

After period of 2-4 years intraabdominal implants grow and rarely they are the cause of seriously mechanical obstruction. Recedive of primary HCC lesion is not contraindication for surgical clearness of diagnosed intrabdominal metastasis.

Long-term survival has been yielded for only selected patients with peritoneal metastasis. Nakayama et al. (14) reported that four patients who survived for more than 1 year after the resection of peritoneal metastasis from HCC had the following feature:

- (1) A small number of metastatic nodules (<4)
- (2) Low serum AFP levels (mean, 205 ng/ml)
- (3) Metachronous occurrence of peritoneal metastases

In conclusion, the resection of peritoneal metastasis from HCC is rare, because of limited indications, but surgical

treatment of these lesions in selected patients may be very beneficial in improving their long-term survival.

CONCLUSIONS:

Hepatocellular carcinoma has tendency to rupture spontaneously which leads to a life treating condition. Non surgical treatment of spontaneously ruptured hepatocarcinoma is method of choice for patients with long-term bleeding and life dangerous clinical parameters. Preoperative diagnosis by US, CT, MRI and angiography, followed by selective segmental arterial embolization may help for the saving of a patient.

Non bleeding patients with stable hemodynamic and confineable MELT levels are indicating surgical resection.

The most observed complications are repeated spontaneous rupture and intraabdominal HCC dissemination. It is not contraindication for resection of primary tumor. Multiples relaparotomies for surgical clearness of abdomen cavity are indicated and they are significant factor for long-term survival.

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