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BENHA MEDICAL JOURNAL

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Published by
Benha Faculty of Medicine

Volume 16 Number 3
Sept. 1999

Benha M. J.
Vol. 16 No 3 Sept. 1999

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Abstract

One hundred twenty eight patiens (112 males and 16 females) were admitted with haemoperitoneum due to ruptured hepatocellular carcinoma (HCC) during the period from January 1995 to January 1999. Their age ranged from 30-70 years with a mean age of 51 years. These patients with emergency presentations were managed according to their hemodynamic state and Child's-Pugh grade. According to the line of treatment we divided the patients into 5 groups. Group 1 consists of 21 patients treated by emergency operative non-resectional maneuvers in the form of diathermy coagulation, suture plication with or without Gelfoam application, packing, or hepatic artery ligation. Group 2 involved 6 patients for whom emergency hepatic resection was done (2 by formal resection and 4 by non anatomical resection). Group 3 consisted of 28 patients treated by transcatheter hepatic artery embolization (TAE) alone. Group 4 included 8 patients treated by delayed hepatic resection following TAE and expectant treatment. Group 5 included the remaining 67 patients treated by conservative (expectant) therapy. The male to female ratio in our series was 7:1. The commonest clinical presentation of ruptured HCC was shock (79.8%). Most of our patients were Child's C (61.7%). The tumor size ranged from 4-21 cm in diameter (mean of 8.5 cm). Abdominal ultrasonography in association with paracentesis achieved the most accurate results in diagnosis of ruptured HCC (sensitivity was 97%). The 1-month mortality rates were reported as 47.6% in

group 1, 33% in group 2, 32.1% in group 3, 0% in group 4, and 68% in group 5. The 1-year survival rates were 9.5% in group 1, 50% in group 2, 10.7% in group 3, 71% in group 4 and 0% in group 5. The long term survival was achieved in the groups of hepatic resection (2-year survival was 16.6% and 42.8% in groups 2 and 4 respectively). Only group 4 recorded 3-year survival of 28,6%. In conclusion, delayed hepatic resection offers the best chance for survival in a certain group of patients who are candidates for surgery. TAE is a safe and effective method for control of bleeding and palliation in ruptured HCC. Conservative treatment is the logical approach in a certain group of patients.

Introduction

Hepatocellular carcinoma (HCC) is one of the most common malignancies in Southeast Asia, Africa and Mediterranean basin (Akriviadis et al., 1998). Mozambique, Zimbabwe, Indonesia, Singapore, China, and Japan were among the high incidence areas (Tang 1999). The median age is 30 years in high incidence areas and 56years in the west. Male predominance is 8:1 in high incidence areas and 3:1 in low incidence areas (El-Bolkainy, 1998). In Egypt, HCC contributes about 2.3% of all cancers with a median age of 53 years and a male predominance of 5:1 (EL-Bolkainy, 1998).

Spontaneous rupture of HCC is a life threatening presentation accounting for 10% of deaths from HCC in Japan (Miyamoto, et al., 1991). About 15% of Asian and African patients with HCC present with this complication where incidence is relatively high (Chearanai et al., 1983). Ruptured HCC tend to occur in patients with tumors located at the periphery, protruding into the abdominal cavity and devoid of overlying liver parenchyma (Kanematsu et al., 1992). Until now the mechanism of spontaneous rupture of HCC has been speculative. The site of bleeding within the tumor is also speculative. It is postulated that acute increase in venous pressure secondary to venous outflow obstruction may occur through direct tumor invasion. This is aggravated in cirrhotics with preexisting portal hypertension (Yamagata et al., 1995). Ruptured HCC causes

bleeding into the peritoneum, resulting in systemic hypotension and hepatic hypoperfusion that may lead easily to hepatocyte necrosis and liver cell failure in cirrhotics, making the prognosis extremely poor (Miyamoto et al., 1991). Because hemorrhagic shock or liver failure accounts for patient death in most cases, the prime therapeutic objective has been hemostasis (Chen et al., 1996). Accurate clinical diagnosis of spontaneous rupture of HCC is often difficult, the prognosis is poor and therapy is far from effective (Zhu et al., 1996). Several treatments have been reported to manage bleeding associated with spontaneous rupture; notably, transcatheter hepatic artery embolization (TAE), microwave therapy, cryotherapy, intralesional alcohol injection, packing or plication and resection (Chiappa et al., 1999). This paper presents our experience in treating spontaneously ruptured HCC in the most recent 128 patients.

Patients and Method

Between January 1995 and January 1999, 128 patients (112 males and 16 females) with ruptured HCC were admitted to the Surgical Emergency Unit and the Surgical Oncology Unit in the Department of Surgery, Mansour Faculty of Medcine. Their age ranged from 30-70 years with a mean age of 51 years. History, clinical examination, assessment of the hemodynamic state, abdominal ultrasound (US) [figure 1], paracentesis, complete liver function tests were done for all patients. Computed tomography (CT) was done for selected group of patients (54 patients) considered to be amenable for interventional methods according to US and Child's Pugh classification for functional hepatic reserve (Pugh et al., 1973). The location of the tumor was detected according to the segmental anatomy of the liver. The patients were divided into 5 groups according to the treatment type of ruptured HCC. Emergency surgical intervention was indicated in 27 patients (group 1 + 2) due to hemodynamic instability and/or persistent bleeding. Group 1, consists of 21 patients in whom urgent midline laparotomies were performed to control bleeding. Hemostasis was tried by diathermy coagulation, suture plication with

or without Gelfoam® application and by packing. Hepatic artery ligation was a must in 11 of these patients. In Group 2, emergency hepatic resection was done for 6 patients (2 by formal resection and 4 by non-anatomical resection). Four of these six patients were Child's B and 2 were Child's A. Operative mortality was defined as death within one month after surgery. Group 3, included 28 patients treated by only emergency TAE. Another 6 patients treated by emergency TAE followed by staged hepatectomy (these 6 patients were included in the group 4 of delayed hepatectomy). Accordingly, a total of 34 patients treated by emergency TAE. These patients have a bilirubin of < 3 mg/dl with absence of complete portal vein thrombosis as evidenced by US. TAE is conducted using a suspension of iodized oil (Lipiodol Ultrafluid; Andre Guerbet, Aulnay-Soubois, France) followed by embolization with gelatin sponge particles (Gelfoam; Ferrosan, Denmark) about 2ml in length injected selectively in the hepatic artery branch that feed the tumor (figure 2: a, b). Group 4 included 8 patients treated by delayed hepatic resection after a mean period of 63 days. Elective surgery was performed following successful TAE in 6 patients and expectant therapy in 2 patients. Five patients of this group were Child's A and 3 were B. Group 5 included 67 patients treated by conservative (expectant) measures. It was logical to manage moribund patients or those with advanced liver disease conservatively. Expectant treatment involved physiological monitoring, fresh blood transfusion, vitamin K infusion, antifibrinolytic therapy, and in some cases with tense ascites controlled taping (1-2 L/day) with albumin infusion was done.

Results

CLINICAL FEATURES: The mean age of patients involved in this study was found to be 51 years and ranged from 30-70 years. The male to female ratio was 7:1.

Presentations: A history of sudden severe epigastric pain was found in 41 patients (33%). History of minor abdominal trauma in 2 patients. Shock was the presen-

tation in 101 patients (79.8%). Picture like peritonitis with abdominal distention was found in 93 patients (72.6%). The presentation may include one or more of these pictures. Table (1) summarizes these presentations.

Child's-Pugh classification: Twelve patients (9.4%) were classified as Child's A, 37 patients (28.9%) as Child's B, and the remaining 79 patients (61.7%) as Child's C.

Size, number and locations of tumors: The maximal diameter size of HCC in this study as detected by US ranged from 4-21 cm with a mean of 8.5 cm. Multiple tumors were detected in 18 cases (14%). Tumors located in the right liver lobe in 81 patients (63.3%), in the lift lobe in 32 patients (25%) and bilateral in 15 cases (11.7%).

INVESTIGATIONS: The diagnostic aids were evaluated through the performed 35 laparotomies. Table (2) shows the results of sensitivity tests for US, US + paracentesis and CT. The ruptured site was diagnosed by US as a hyperechoic area located around the tumor in 87 patients (67.2%) as shown in figure (1). Paracentesis was positive for blood in 98% of ascitic patients (99/101) and in 81.5% of the non-ascitic patients (22/27).

TREATMENT METHODS:- We reported the results of treatment in each group.

Group 1 : Emergency Operative Non-Resection Maneuvers: - Diathermy coagulation using blunt tip failed to control bleeding alone in all cases (4 patients), while suture plication with or without Gelfoam application controlled bleeding in 50% (7/14) of cases (2 of them failed to be controlled by diathermy alone). Hepatic artery ligation controlled bleeding in 63.6% (7/11) of cases (8 of them failed to be controlled by previous measures). Packing controlled bleeding in 60% (3/5) of cases (3 of them were uncontrollable by previous measures). Two patients died in the theater due to uncontrolled bleeding. Operative mortality (within 1 month) reported in 8 cases; 5 due to liver cell failure and the other 3 patients died from hepatorenal syndrome. The l-

month mortality rate of this group was 47.6%. Eleven patients (52.4%) survived for periods ranged from 3-15 months with a median of 5.5 months. The one-year survival rate for this group was 9.5%. Table (3) shows the operative procedures and the outcome of these 11 patients.

Group 2 : Emergency Liver Resection: The mean time from admission to surgery was 140 min (range: 125-170 min) and the mean estimated volume of intraperitoneal blood was 1700ml (range: 1300-2700ml), Bisegmentectomy VII & VIII was performed in one patient and bisegmentectomy II & III was done in another one. Non-anatomical wedge resection was done in the other 4 patients. Two patients died at 10 and 19 days after surgery from hepatorenal syndrome and liver cell failure respectively. Two patients died at 9 and 16 months after surgery from tumor recurrence. Two patients are alive and disease free at 18 and 30 months after surgery. The l-month mortality rate was 33%. The l-year survival rate of this group was 50% and 2-year survival rate was 16.6%. Details of operative findings and outcome are shown in table (4).

Group 3 : Treatment with TAE-alone: All patients underwent emergency TAE within 24 hours after admission. Vascular tumors were present in all 34 patients (figure 2, a) but extravasation of the contrast medium from the ruptured HCC was seen in only 6 patients (17.6%). TAE led to successful hemostasis in 31/34 patients (91%), as judged by disappearance of extravasation, occlusion of tumor feeding vessels, or stabilization of vital signs (figure 2, b). Major complication was noted in one patient who had impaired renal function. He experienced acute renal failure, which was treated successfully by conservative measures. Minor complications, so called postembolization syndrome (fever, pain, and increase in transaminase level), were observed in all patients. These complications subsided within 1-3 weeks after TAE in the majority of patients. Of the 28 patients treated solely with TAE, 9 patients died within 1 month (l-month mortality rate was 32.1%) and only 3 patients sur-

vived for more than 1 year (1-year survival rate was 10.7%). Re-rupture occurred in 7 patients (25%).

Group 4 : Delayed (Elective) Hepatic Resection: Following successful control of bleeding by TAE the patients were prepared for elective resection. The mean period of delay was 63 days (average 21-105 days). Left lobectomy (segmentectomy II, III, IV) was performed in 2 patients (figure 3-a, b). Right lobectomy (segmentectomy V, VI, VII, VIII) was performed in one patient, bisegementectomy (II, III, and VII, VIII) in 2 patients and marginal resection in 3 patients. No operative mortality was recorded in this group. Three patients died at 11,15 and 27 months from tumor recurrence. One patient died at 8 months from liver cell failure. Four patients are living at 42, 37,12, and 6 months. One-year survival rate for this group was 71% (the last patient was excluded as the follow up period was only 6 months). Two-year and 3-year survival rates were 42.8% and 28.6% respectively. Details of operative procedures and outcome are shown in table (5).

Group 5 : Conservative (Expectant) Treatment: Forty six patients died within one month after admission (1-month mortality rate was 68%). Delayed hepatic resection was performed in 2 patients who are considered to get curative resection after period of 40 and 63 days. No patient of the remaining 19 patients survived for up to 1 year.

THE OUTCOME: The 1-month (operative) mortality rate of elective resection group (0%) was significantly better than other groups. The worst was that of conservative treatment group (68%). On the other hand the survival rates of all groups, described by the chart in figure (4), showed a better survival rates in the resection groups mostly in the elective hepatectomy group.

Table 1 : Summar y of the presentations of ruptured HCC .

Association	Pain		Shock		Peritonism	
	No.	%	No.	%	No.	%
Alone	3	2.4%	23	18%	4	3.2%
Shock (Sh)	8	6.2%	-	-	59	46%
Peritonism (Perit)	19	14.8%	59	46%	-	-
Pain (P)	-	-	8	6.3%	19	14.8%
Sh. + perit	11	8.6%	-	-	-	-
P + Sh.	-	-	-	-	11	8.6%
P + Perit	-	-	11	8.6%	-	-
Total	41	33%	101	78.9%	93	72.6%

Table 2 : Sensitivity of diagnostic aids in detection and localization of ruptured HCC. as confirmed by 35 laparotomies .

Diagnostic Method	Diagnosis of Ruptured HCC		Accurate Localization of Tumors	
	No.	Sensitivity	No.	Sensitivity
Abdominal US	23/35 ptn.	65.7%	25/35	73.5%
US + Paracentesis	34/35 ptn.	97.1%	-	-
CT	19/21 ptn.	50.5%	20/21	90.4%

Table 3 : Operative results and outcome of the 11 patients survived after emergency laparotomy in Group 1.

Ptn no.	Age/y	Child's Pugh	site of Tumor	Procedure	Outcome /month
2	47	C	INF	HAL	3
4	56	C	INF	HAL	3.5
5	60	B	SUP	suture plication + Gelfoam	7
6	70	B	SUP	suture plication + Gelfoam	4.5
9	59	C	SUP	HAL + Packing	5.5
10	45	B	SUP	diathermy + suture plication	15
12	49	C	INF	suture plication + HAL	6.5
14	48	C	SUP	Packing	4
15	50	B	SUP	diathermy + suture plication	4
18	54	B	SUP	suture plication + Gelfoam	13.5
19	60	C	INF	suture plication + Gelfoam	8.5
Total/11 Median/54y		5B / 6C	7 sup/4 inf		5.5m

Table 4 : Operative findings and outcome of emergency hepatic resection (Group 2).

Ptn no.	Age/y	Child's Pugh	Tumor location	Type of resection	Tumor size resection	Intraperit. estimated. Blood/ml	Recurr-ence	Outcome/ month
1	35	A	VI	limited	7 cm	1400	liver	16
2	56	B	VII, VIII	bisegment	11 cm	2700	-	died 10 d.
3	49	B	VII	limited	5.5 cm	1400	non	30
4	53	B	II, III	limited	6.5 cm	1600	peritoneal.	9
5	42	A	II, III	bisegment	5 cm	1300	non	18
6	65	B	VIII	limited	9 cm	1800	-	died 19 d
mean/50					7.3 cm	1700		12 m

Table 5 : Operative findings and outcome of delayed hepatic resection (group 4).

Ptn no.	Child's Pugh	Tumor location	Resection	Tumor size (cm)	Recurrence	Outcome/ in month
1	B	II, III	Lt. Lobctomy	15	liver (at 15m)	27* (died)
2	A	III	limited	5	non	42 (alive)
3	A	VIII	bisegment	7	liver (at 27m)	37 (alive)
4	B	VI	limited	8.5	liver (at 9m)	15* (died)
5	A	VII, VIII	Rt. Lobectomy	11	-	8# (died)
6	B	II, III	bisegment	9	perit. (at 6m)	11 (died)
7	A	VI	limited	4	non	12 (alive)
8	A	VIII	limited	6.5	non	6 (slive)
Mean				8.25		21.5 m

*: The two patients treated by expectant treatment. #: died from liver cell failure .

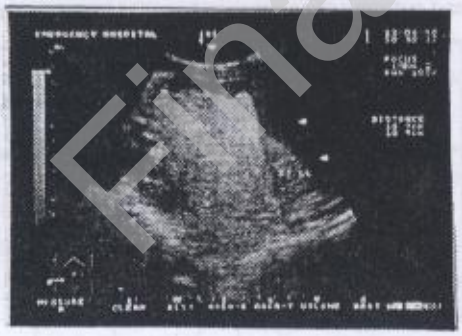

Fig. 1 : Ultrasnography of a ruptured HCC showing the mass in the right lobe with hyperechoic areas of blood around .

Fig. 2-A : Hepatic artery angiography showing vascular tumor in left liver lobe (TAE before treatment) .

Fig. 3-A : The specimen of left lobectomy.

Fig. 2-B : TAE after successful embolization showing complete occlusion of the feeding artery.

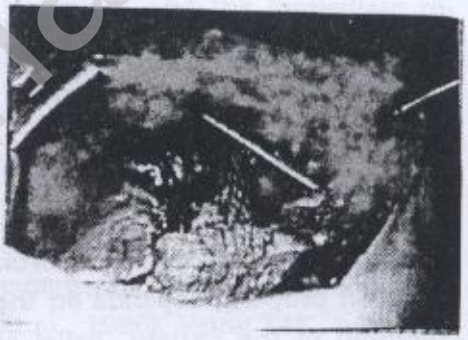

Fig. 3-B : The remaining liver after left lobectomy .

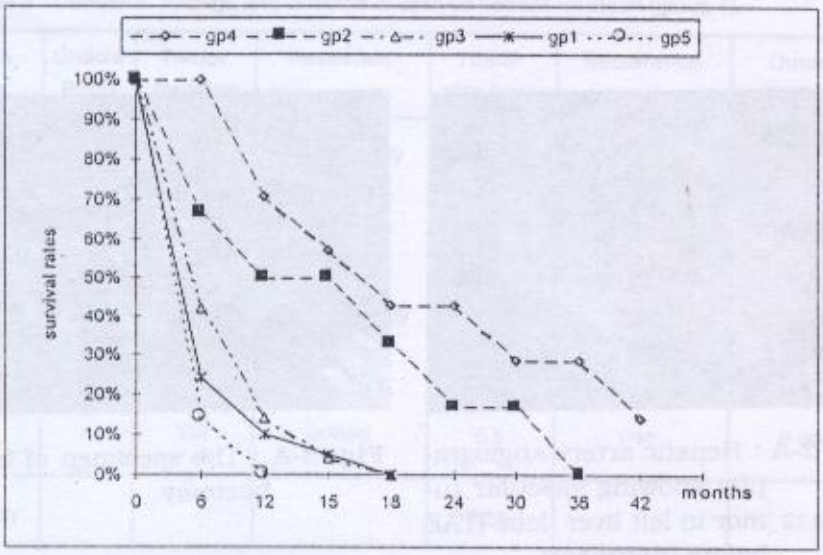

Fig. 4 : Chart for comparison between survival rates in all groups.

Discusion

As there are few reports on ruptured HCC complicating cirrhosis there is no general agreement on the standard treatment (Chearanai et al., 1983 & Lai et al 1989). Accordingly the criteria of selection for patients for different procedures have not been rigidly formulated in previous reports. Selection properly depends on the condition of the patient, belief of surgeon, availability of interventional radiology and whether or not laparotomy has been undertaken.Comparison of results of different treatments is, therefore difficult (Zhu et al., 1996).

The present study shows the results of the policy followed in Mansoura Emergency Hospital for the management of ruptured HCC during the last 4 years. Mansoura Emergency Hospital - where the Surgical Emergency Unit presents- is a referral hospital for emergency cases. That is why we have experienced a marked increase in the number of such cases since 1995 (the date of opening of that hospital). The general sur-

geons in collaboration with the oncologic surgeons and the interventional radiologist were concerned in the management of ruptured HCC.

Shock was the commonest (79%) presenting feature in our series. So, it was logical to start with supportive measures in all patients to achieve hemodynamic stability, and to guard against developing of hepatorenal syndrome and/or liver cell failure in these friable patients with liver cirrhosis (Lai et al., 1989, Dewer et al., 1991). These supportive measures (conservative treatment) was continued as the sole emergency therapy for the major sector (53%) of our patients. The conservative treatment has been adopted by many surgeons when the patient is moribund or as a 'wait-and-see' policy for those who are judged unlikely to tolerate an invasive procedure (Xu and Yan., 1994). The reported results of conservative treatment are, therefore, generally poor, the hospital mortality rate was 85% by Cheranai et al. 1983, and 68% in the present study. However, some patients are hemodynamically stable on presentation or after resuscitation. For them it is doubtful whether any urgent and invasive procedure is necessary. Irrespective of policy, conservative treatment should be a part of an active treatment process that prepares the patients for operative or non-operative intervention (Zhu et al., 1996).

Hemostasis is essential to consolidate the hemodynamic stability. Shuto., et al., 1998, reported 70% (7/10 patients) hemostasis by conservative treatment alone. In the present study hemostasis was possible in 35% (45/128) of cases by conservative treatment alone. In one study, conservative treatment was adopted as the first treatment and the immediate results were not inferior to those of emergency surgery (Xu and Yan, 1994). The interventional methods to accomplish hemostasis ranges from the minimally invasive TAE up to the major procedure of emergency hepatic resection (Zhu et al., 1996). Using TAE, hemostasis is achieved in 75%-100% (91% in this study) of patients, but recurrent bleeding and hepatic failure may occur (Okazaki et al., 1991). To reduce negative effects

on the functional liver reserve, emergency TAE should be conducted as selectively as possible and better avoided in patients with main portal vein thrombosis (Shimada et al.,1998). To prevent recurrence of bleeding TAE can be repeated every 3-4 months as recanalization of the hepatic artery may occur. This is applicable only in case of Gelfoam® embolization (Hsieh et al. 1987). Okazaki et al., 1991, concluded that TAE should not be done if total serum bilirubin was > 3 mg/dl and this conclusion was confirmed by the work of Ngan et al.,' 1998. The hospital mortality rate of TAE alone was reported by Hsieh et al., 1987 to be 29.4% (32.1% in this study). On the other hand, using hepatic artery ligation, effective hemostasis was achieved in 68.1-100% (63.6% in this study) and hospital mortality rate was 67-76.6% (Lai et al., 1989, Dewar et al., 1991). Suture plication is unlikely to be applicable to bleeding points that are multiple or located at inaccessible site or to large friable tumors (Zhu et al., 1996). Packing is feasible for tumors located under the diaphragm, because the diaphragm exerts a tamponade effect. Overall, Packing is effective in controlling bleeding in about 80% of cases (60% in this study), but carries the risk of rebleeding after removal of the packs within 24-48 hours after surgery (Zhu et al., 1996).

Although the above measures could be effective for hemostasis of ruptured HCC, rebleeding rates of these non-resectional techniques are high as the source of bleeding (the tumor) still in place and progressing. Hepatic resection in those patients with acceptable hepatic reserve appears to be the treatment of choice offering the only chance for cure (Chen et al., 1988). Emergency (one-stage) hepatectomy may seem to be ideal for these purposes if it can be accomplished quickly, especially if the tumor is peripherally located or is pedunculated. However, in a patient who requires formal lobectomy, the length of time required, blood loss induced and resection of adjoining functioning liver parenchyma may actually accentuate the problem of liver failure (Zhu et al., 1996). Yoshida et al., 1999, reported operative mortality rate of 33% and 50% respectively

(33% in this study). The 1-year survival rate for this group was 50% in our study, similar to that reported by Chiappa et al., 1999. However, long term survival rate are generally poor, as the operation is performed without the advantage of detailed investigations to delineate the extent of tumor within the liver, the resection margin is often positive for malignancy leading to tumor recurrence (Dewar et al., 1991)

The combination of acute hemorrhage with cancer requires a two-stage therapeutic approach. First it is important to accomplish hemostasis and, stabilize cardiorespiratory reserve, evaluate hepatic reserve, and accurately staging the HCC. Second, it is advisable to perform a two-stage hepatectomy (Yoshida et al, 1999). Zhu et al., 1996, reported that the rational treatment for the majority of patients with ruptured HCC was TAE, followed by hepatectomy if the lesion was resectable. In the present study we reported a 0% operative mortality rate for delayed resection, this was similar to that reported by Shimada et al., 1998. The 1-year survival was 71% in this study which was similar to that reported by Shuto et al.,1998 (77%). However, Shuto et al., 1998, reported a better 3-year survival rate (48%) in comparison to our study (28.6%). This might be attributed to the larger tumor size in our study (mean 8.25 cm) as compared to their study (mean 7.5cm). Also the use of adjuvant treatment in their study might improve the survival.

Abdominal ultrasonography is valuable in the diagnosis of ruptured HCC because it is simple quick and non-invasive (Zhu et al., 1996). The ruptured site appears as a hyperechoic area located around the tumor in 66% of cases (Corr et al., 1993). Abdominal paracentesis is positive in 86% of patients (Miyamoto et al., 1991). So, it was logical to combine US and US-guided paracentesis to diagnose ruptured HCC in our study. This simple, rapid and applicable combination gives a sensitivity of 97%. On the other hand CT has a better resolution for localizing tumors than US. CT can demonstrate a peripheral hepatic tumors and shows free intraperitoneal fluid with areas of high

attenuation close to the tumor, representing acute blood clotting, in almost every case (Pombo et al., 1991).

In conclusion, delayed hepatic resection offers the best chance for survival in certain group of patients who are candidates for surgery. TAE is a safe and effective method for both control of bleeding and palliation in ruptured HCC. Conservative treatment is the logical approach in a certain group of patients.

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