Original Paper

Emergency Embolization in the Treatment of Ruptured Hepatocellular Carcinoma Following Transcatheter Arterial Chemoembolization

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KEY WORDS:
Carcinoma; Hepatocellular; Chemoembolization; Rupture; Life–threatening complications; Emergency embolization

ABBREVIATIONS:
Hepatocellular Carcinoma (HCC); Transcatheter Arterial Chemoembolization (TACE); Alpha–Fetoprotein (AFP); Computed Tomography (CT); Standard Deviation (SD)

ABSTRACT

Background/Aims: Rupture of hepatocellular carcinoma (HCC) following transcatheter arterial chemoembolization (TACE) is a rare and life-threatening complication. The purpose of the present study was to evaluate the utility of emergency embolization for treatment of ruptured HCC following TACE.
Methodology: Five patients developed rupture of tumor after TACE in 1005 patients of HCC from October 2007 to February 2010, and were studied retrospectively. Emergency selective arterial embolization was performed in all 5 patients because of intractable hemorrhage in the peritoneal cavity or around the liver that could not be controlled by conservative method. The mean hemoglobin level before embolization was 75.6g/L±20.7 (mean±standard deviation).
Results: Hepatic angiography did not revealed extravasation of contrast from the tumor in all 5 patients with rupture of HCC following TACE. After selective embolization of feeding arteries of the liver tumor, intraperitoneal bleeding from HCC was stopped immediately in all patients. The mean hemoglobin level after embolization in 48 hours was 102.6g/L±13.5. No severe complication related to emergency embolization was found after treatment.
Conclusions: Emergency arterial embolization is effective for hemostasis of ruptured HCC following TACE in patients with hemodynamically unstable condition.

INTRODUCTION

Hepatocellular carcinoma (HCC) is one of the most common malignant tumors occurring in the liver in the world, which is the third leading cause of death from cancer worldwide (1, 2). Studies have shown that South-East Asia regions, including China, have a higher incidence rate of HCC, because of the endemic nature of hepatitis B and C in those countries (2, 3). Surgical interventions including complete surgical resection and liver transplantation demonstrate potentially curative treatment options when the tumor is restricted to the liver, and offer the best prognosis for HCC. However, only 15%–30% of patients with HCC are surgical candidates due to advanced liver disease, extrahepatic metastases, or inadequate functional hepatic reserve and poor general condition of the patient (4, 5). Transcatheter arterial chemoembolization (TACE) is the most widely used primary treatment in patients with hepatocellular carcinoma (HCC) who are considered to be unsuitable candidates for surgery (6). Although satisfactory survival results can be achieved with TACE, it is associated with complications causing significant morbidity and mortality. Fever, biliary injury, neutropenic sepsis, and liver failure are well recognized complications (7, 8). However, to the best of our knowledge, the management of HCC rupture, a fatal complication with high mortality rate following TACE, has rarely been reported. The incidence is very low, ranging from 0.15% to 0.68% (9, 10). High rates of successful hemostasis have been achieved with arterial embolization in the management of spontaneous rupture of HCC (11). Thus, the purpose of this research was to evaluate the role of emergency embolization in the treatment of ruptured HCC following TACE.

METHODOLOGY

This study was approved by our local institutional review board and performed in a large surgical center. A retrospective analysis was performed in 1005 patients of HCC who received TACE from October 2007 to February 2010. Of these, 5 patients developed rupture of tumor after TACE (incidence 0.50%). There were 2 men and 3 women. Ages

ranged from 28 to 83 years (mean, 50 years). They had a confirmed diagnosis of unresectable HCC which was established based on the high serum alpha-fetoprotein (AFP) value, tumors observed at computed tomography (CT) scan and clinical evidences. The interval between TACE and tumor rupture was 16 hours to 7 months. Rupture of the HCC was verified by the presence of hemorrhage in the peritoneal cavity on abdominal paracentesis in all 5 patients. Additionally, hemorrhages in the peritoneal cavity or around the liver were revealed on the emergency CT scan. Rupture occurred in 3 patients who had already undergone 1 session of TACE using an emulsion of iodized-oil (Lipiodol; Guerbet, Aulnay-sous-Bois, France) and anticancer drugs. The HCC ruptured spontaneously post 2 session of TACE in 2 patients. The size of the ruptured HCC following TACE varied from 7 to 14 cm in maximum diameter (median, 11cm). The mean hemoglobin level of the patients was 75.6g/L±20.7 (mean±standard deviation). The clinical parameters are summarized in **Table 1**.

Both hepatic and superior mesenteric digital subtraction angiography was performed in all 5 patients before emergency transcatheter arterial embolization. Depending on the arterial supply of the tumor and the bleeding point identified by the arteriography, the catheter was superselectively placed into the feeding arteries for selective embolization. The iodized-oil was injected into tumor feeding arteries until all parts of the tumor were filled with it. Gelatin sponge particles, approximately 1 mm in size, were injected until the arterial blood supply to the tumor was completely stopped.

An angiography was performed post embolization to ensure the complete occlusion of the vessels. All 5 patients were transferred to the intensive care unit for further observation. Therapeutic effect of emergency embolization was defined as stabilization of hemodynamic condition and hemoglobin level for at least 48 hours after treatment.

Statistical analyses were conducted with SPSS software (SPSS for Windows, version 11.0, 2001; SPSS, Chicago, Ill). Values are expressed as mean±standard deviation (SD). Difference between the mean hemoglobin levels of the patients pre- and post- the emergency embolization were analyzed using a paired t test. A two sided p value of less than 0.05 was considered statistically significant.

RESULTS

Ruptured HCCs following TACE were demonstrated on the emergency CT in all 5 patients in present study. The presences of blood in the peritoneal cavity or around the liver were found on CT images which confirmed tumor rupture (**Figure 1**.). Vascular HCCs were found in the emergency hepatic angiography in all 5 patients. However, hepatic angiography did not reveal extravasation of contrast from the tumor indicating active bleeding from the HCC (**Figure 2**.). The portal vein, without filling defect or obstruction, was seen in all 5 patients, while arterioportal shunting was not found. After successfully selective embolization of feeding arteries of the liver tumor, intraperitoneal bleeding from the HCC was stopped immediately in all patients. All the patients left the angiography room in a stable condition after the procedure was terminated. The mean hemoglobin level after embolization in 48 hours was 102.6g/L±13.5. Difference between the mean hemoglobin level of the patients pre- and post- emergency embolization was statistically significant (p=0.006).

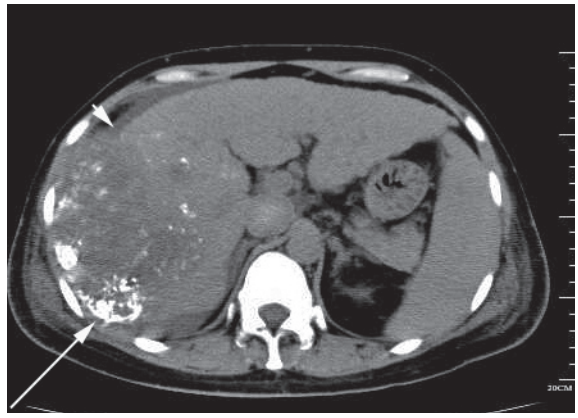

FIGURE 1
Conventional CT scan of liver shows ruptured HCC (long arrow) in right lobe of liver with adjacent blood clot (short arrow) in the peritoneal cavity and around the liver.

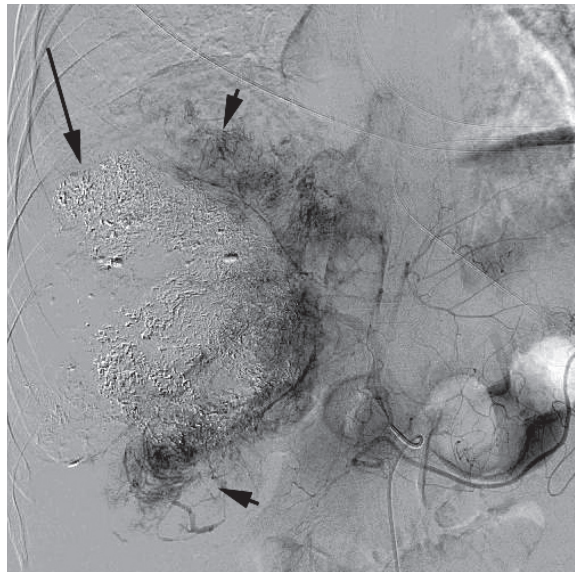

FIGURE 2
Hepatic angio–graphy shows a partially embo–lized HCC (long arrow) with partial abnormal stain (short arrows) in the right lobe. There is no ap–parent extravasa–tion of contrast from the tumor to peritoneal cavity.

No severe complication related to emergency embolization occurred until they were discharged. Four patients recovered and were discharged uneventfully. One 83 years old woman died with respiratory failure 1 week after embolization procedure. Her cause of death was unrelated to the embolization procedure.

DISCUSSION

The incidence of HCC is increasing in the world mainly because of the rise in hepatitis B and C infections (2, 4). Hepatic resection or transplantation is restricted to a small minority (25%-30%) of patients (12, 13). In our days, TACE therapy has already become a very important commonly used treatment

TABLE 1 Clinical Parameters of the Patients

Variables	Case 1	Case 2	Case 3	Case 4	Case 5
Sex	F	F	F	M	M
Age	28	42	83	51	47
Location of the tumor	Right Lobe	Right Lobe	Right Lobe	Right Lobe	Right Lobe
Size of tumor (cm)	13	11	14	7	10
Exophytic growth	Yes	Yes	Yes	Yes	Yes
Sessions of TACE	2	1	1	1	2
Interval between TACE & rupture	1 month	3 days	5 months	16 hours	7 months
hemoglobin level pre-embolization (g/L)	90	66	104	54	64

which provides survival benefit for selected patients with HCC (14, 15). It is also the most extensively used treatment for patients on the waiting list for liver transplantation. The suspension consists of iodized-oil and anticancer drugs have been one of the most effective agents (16). After selective catheterization of feeding artery of the tumor, the suspension is slowly injected into the target vessel in order to fulfill the microcirculation of the tumor and stay there for long time to stop the blood flow which causes tumor necrosis (17). It is well known that the common complications related to TACE are postembolization syndrome (abdominal pain, fever, vomiting, and nausea), leuko-cytopenia, and impaired liver function (18, 19). There are several severe and rare complications of TACE including neutropenic sepsis, liver failure, perforation of duodenum, pulmonary embolism, bilioma, acute renal failure and liver abscess, which are associated with significant morbidity and mortality (18, 20). So the treatment-related mortality of TACE is 4.1% (19).

Spontaneous rupture is a life-threatening presentation of HCC. The incidence is from 3% to 14.5% according to the reports (11). TACE is the treatment of choice for the emergency management of spontaneous rupture of HCC (11). However, rupture following TACE is a rare catastrophic complication of HCC and has a high mortality rate (11). The reason of rupture of HCC following TACE is unclear. It could be related to tumor necrosis and increased pressure inside the tumor after treatment. The large HCC lesions are considered to be at increased risk of rupture as they are more likely to contact the liver surface (9, 20). In addition, it could be speculated that vascular damage occurring in the pathological vessels of the hepatoma following TACE might result in tumor rupture and bleeding into the peritoneal cavity. (9, 20) As far as the authors are aware, there are few reports of the management of HCC rupture following TACE (21).

The mortality and morbidity rate of HCC rupture following TACE is high because the patients often have a poor liver function and advanced disease. The emergency objective in the treatment of these patients is to achieve hemostasis in time by conservative, surgical, or non-surgical methods. Conservative therapy has been justified for selected patients in hemodynamically stable condition or in extremely poor condition, but a high mortality rate due to continuous bleeding or rebleeding after conservative treatment has been reported (10). Although immediate hemostasis has been achieved with surgical methods, the associated mortality rates have been high (21). From the experience in our center, a repeat emergency arterial embolization could be performed to achieve immediate hemostasis and stabilize the tumor.

In conclusion, ruptured HCC following TACE is a rare and fatal complication. Emergency arterial embolization is effective for hemostasis of ruptured HCC following TACE in patients in hemodynamically unstable condition.

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