

RUPTURED HEPATOCELLULAR CARCINOMA FOLLOWING TRANSCATHETER ARTERIAL CHEMOEMBOLIZATION

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Transcatheter arterial chemoembolization (TACE) is known to be an effective palliative treatment in unresectable hepatocellular carcinoma (HCC). Although TACE can control tumour growth and palliate the patients, complications of TACE with significant morbidity are well known and adversely affect the outcome of patients. Necrotic tumor rupture is a serious complication of TACE and has a high mortality rate. We report a case of ruptured HCC following TACE in a 78-year-old male patient who subsequently developed peritonitis and pneumoperitoneum. This case gives us the opportunity to underline the importance of such complications and demonstrates the utility of CT imaging for diagnosis and management of patients with ruptured HCC.

Key-word: Liver neoplasms, therapy.

Hepatocellular carcinoma (HCC) is one of the most common cancers in the world. It is a growing public health problem and its incidence is increasing worldwide (most cases of HCC in Asia and sub-saharan Africa but recently, in western countries too (1, 2)). The presence of cirrhosis is the major risk factor, essentially due to chronic hepatitis C and hepatitis B infection or alcohol disease (1). Hepatocellular carcinoma is of poor prognosis: the five-year survival rate is less than 5 percent (2). The prognosis depends on hepatic function, tumour size, and tumour extent at the time of diagnosis. Nowadays, orthotopic liver transplantation only remains curative, but because of the shortage of organ donors, these treatments are applicable only to a small part of all patients. The majority of the patients with unresectable HCC are treated by various palliative therapies included surgical resection (partial hepatectomy), or percutaneous treatment. Despite advances in imaging techniques and follow-up programs only 20% of patients are candidates for surgery at the time of diagnosis (3, 4) due to an advanced tumor stage, comorbidities, poor hepatic functional reserve or shortage of donor livers.

Case report

A 78-year-old man was referred to our hospital in September 2008 for a health deterioration associated with weight loss. His medical history was

remarkable for silicosis associated with respiratory failure, type 2 diabetes and cerebrovascular accident. He had a previous history of smoking and persistent alcohol abuse was documented. On admission, his height was 165 cm and his body weight 74 kg. There was no history of hematemesis, vomiting, flushing or diarrhea.

Clinical examination revealed a hepatomegaly without splenomegaly. Jaundice, ascites, peripheral oedema and other signs of chronic liver disease were not observed. The patient's blood pressure was 120/60 mmHg and heart rate was regular to 74 beats per minute. Laboratory test revealed marked leukocytosis (18000/mm³), hemoglobin level 11g/dl and abnormal liver function tests (ALP/GGT: 125/158 IU/L). Serum tumor markers were within normal range (-fetoprotein: 2.6 ng/ml). Other laboratory tests were also within normal range. However, glycaemia (110 mg/dl) and HbA1c (7.9%) were slightly elevated. Tests for hepatitis B and C virus markers were all negative. The patient showed a Child-Pugh score of 7 (class B).

A triphasic contrast enhanced CT-scan showed three hypervascular lesions, without clear wash out, suspected of malignancy. The bigger one was in segment IV (4 × 4 cm) and near to the liver capsule. The other lesions were localized in segment II and in segment VI. Ultrasound was not contributive because of patient's corpulence. A

CT-guided biopsy of the largest hepatic lesion (segment IV) confirmed the diagnosis of well differentiated HCC in a cirrhotic liver. The patient was medically treated.

On a follow-up CT scan, a few months later, it appeared that the segment IV mass was markedly increased (6 × 5.5 × 7 cm) (Fig. 1A). The segment II and VI lesion were confirmed but stable. Additional tests did not reveal any metastasis.

After multidisciplinary consensus and given the patient's delicate clinical condition, surgical treatment was not adequate. In these conditions, the presence of multiple liver HCC nodules justified a transarterial chemoembolization (TACE). TACE was performed with no intra-operative complications. Embolization of the feeding artery was performed with small gelfoam pledgets before (to reduce the flow) and after (to achieve stases) injection of 50 mg of cisplatin (Fig. 1B and C). Post-operative and one week control CT-scan (Fig. 2) didn't show any sign of active arterial contrast extravasation and other complications.

Three weeks after transarterial chemoembolization (TACE), the patient complained about a right upper abdominal pain. This led to an abdominal CT-Scan (Fig. 3) that revealed ruptured necrotic mass with associated peritonitis and pneumoperitoneum but no active bleeding. At this time, laboratory test revealed stable anemia (haemoglobin level: 10.9 g/dl), hypoalbuminemia (19 g/l), abnormal liver function tests (ALP/GGT: 359/168 IU/L) and elevated conjugated bilirubin level (5.2 mg/L).

Because of the bad general state of the patient, conservative treatment was decided with discharge from hospital to palliative care. Unfortunately, the patient died two months after TACE procedure.

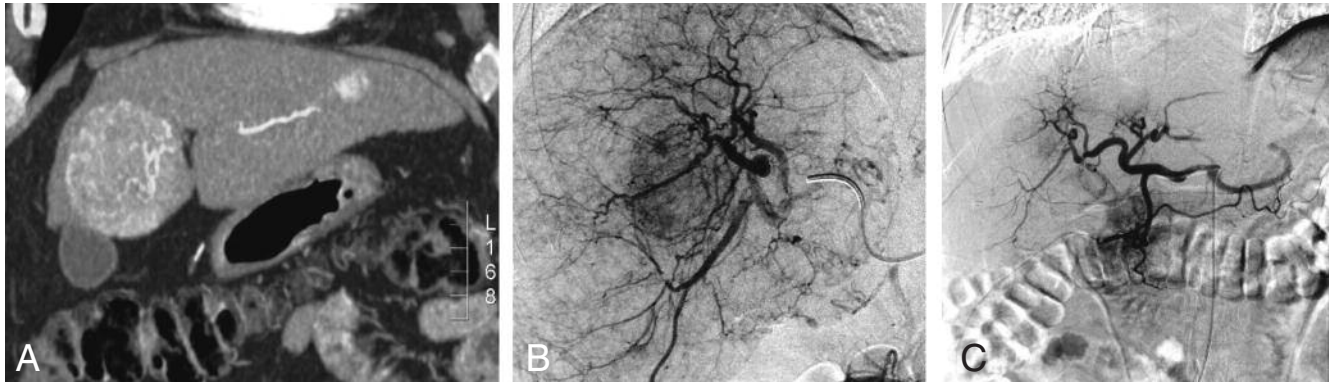


Fig. 1. — A: Coronal Multi-Planar Reconstruction (MPR) of a contrast enhanced CT scan of arterial phase demonstrates a hyper-enhancing lesion in segment IV. B: Hepatic angiography (arteriogram) shows an anarctic hypervascularised hepatic mass that suggests hepatocellular carcinoma with formation of arteriovenous shunts. C: Hepatic angiography after chemoembolization shows an almost complete regression of the anarctic vascularisation in the lesion.

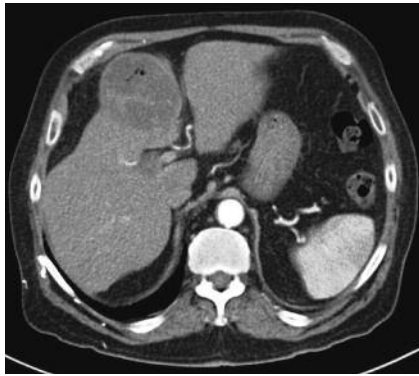


Fig. 2. — Contrast enhanced CT scan obtained one week after TACE shows the integrity of the liver capsule.

Discussion

Transarterial chemoembolization (TACE) is an efficient palliative well accepted treatment for unresectable HCC (3, 5, 6). In the presence of multiple HCC nodules, TACE remains the

treatment of choice (7). TACE combines the effect of targeted chemotherapy with the effect of ischemic necrosis induced by arterial embolization (8). The basic principles of the procedure consist of a reduction of hepatic arterial blood supply to the tumor as well as the delivery of cytostatic agents (Adriamycin, Cisplatin, or Doxorubicin) directly into the tumor. It is well known that HCC is hypervascularised (with a high propensity for vascular invasion and growth factor produce) and that this hypervascularisation is mostly dependent on the hepatic artery and its branches (9).

The survival benefit of this treatment is confirmed by two meta-analyses (10, 11) and two recent randomized controlled trials (4, 12) that allowed showing a significant higher survival rate compared to a group of best supportive care after three years. However its benefic appears only in selected patients with unresectable HCC and preserved liver

function. Tumor sizes, hypovascularity on imaging and elevated INR are predictors of increased mortality after TACE therapy for HCC (13). Contraindications for TACE (19) include portal vein thrombosis, significant arteriovenous shunting and poor liver function (Child-Pugh class C).

Imaging techniques and correct anatomical evaluation is essential to select those patients who may potentially benefit from the procedure. CT or MR examinations should be done prior to TACE (8). Although mean survival rates of 12 months (13) have been reported, a variety of complications have been described after TACE with significant morbidity. These complications are more often benign and include postembolization syndrome (fever, abdominal pain, nausea, and vomiting), impaired liver function, and leukocytopenia (3, 5, 14). However major complications are described. Liver failure, as well as liver abscess, splenic infarction,

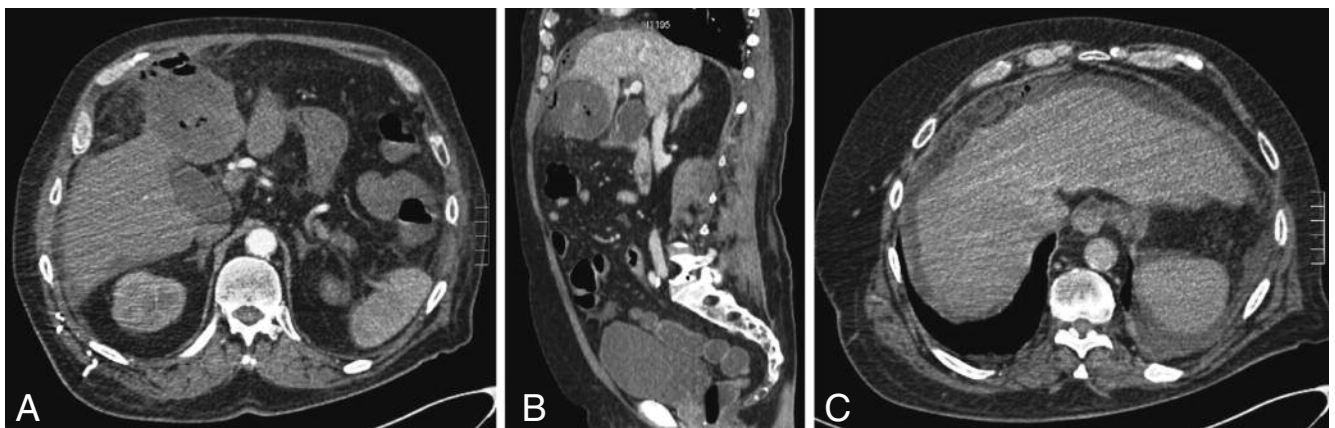


Fig. 3. — Axial (A and B) and sagittal (C) contrast enhanced CT scan, in arterial phase, obtained 3 weeks after TACE shows a capsular rupture at the level of the necrotic mass with associated peritonitis and pneumoperitoneum.

upper gastrointestinal bleeding, bile duct complications, acalculous cholecystitis, pulmonary embolism, spasm or occlusion of hepatic artery and acute renal failure are associated with significant morbidity and mortality.

Rupture following TACE is uncommon and represents less than 1% of all complications (15) but it is probably the most important complication of TACE with an extremely poor prognosis (1). The mortality and morbidity rate is high because the patients usually suffer from an advanced disease.

The mechanism of rupture of HCC after TACE is unclear. It is probably to be related to tumor and capsular necrosis and increased pressure inside the friable tumor after TACE. Secondary infection, vascular injury during TACE or inflammation secondary to the chemotherapeutic agents could play a role too (1). They can appear especially when there is no tumor capsule or when the lesion is located adjacent to the Glissonian liver capsule (16). Two series from Asia conclude that most patients with complications after TACE had pre-existing risk factors as large tumor size, or extracapsular extension of the tumor (15, 17).

Patients with ruptured hepatocellular carcinoma present right upper abdominal pain and abdominal distension and the diagnosis is usually confirmed by US or CT-Scan. CT imaging is the most useful modality in the imaging of HCC (18) and can detect most of complications following TACE (18). In a ruptured HCC, blood or gas (as a result of necrosis) may be seen in the lesion, around the liver or within the peritoneal cavity. Bleeding may also occasionally be seen.

Management of patients with rupture of HCC following TACE is difficult and remains controversial because patients have already been diagnosed as having inoperable tumor and poor liver function. The primary objective in the management of these patients is to control potential bleeding and to maintain haemodynamic parameters stable. Hemostasis can be done by surgical laparotomy, interventional or conservative methods. Battula et al (19) consider that a repeat TACE can be

performed to stabilize the tumor. In our opinion, emergency embolization is an efficient haemostatic treatment in case of intra-peritoneal bleeding of a ruptured HCC. In this particular situation of our patient with a bad general health and the absence of active bleeding, TACE or embolization had to be excluded. The only left solution was conservative management.

Although TACE is generally a safe procedure, tumor rupture remains a potential complication. As showed in our patient, it appears to be especially important in large tumors adjacent to the liver capsule. In case of such important masses, liver rupture is a clear but relatively rare complication that may occur even in absence of TACE. This complication may appear relatively lately (several weeks) after procedure, that the reason why a precise follow-up is mandatory.

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