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CASE REPORT

Complete hepatocellular carcinoma necrosis following sequential porto-arterial embolization

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Abstract

Most patients with hepatocellular carcinoma (HCC) are not eligible for curative treatment, which is resection or transplantation. Two recent series have emphasized the potential benefits of preoperative arterio-portal embolization prior to surgical resection of such tumours. This preoperative strategy offers a better disease free survival rate and a higher rate of total tumor necrosis. In case of non resectable HCC it is now widely accepted that transarterial chemoembolization (TACE) leads to a better survival when compared to conservative treatment. Thus, the question remains whether combined portal vein embolization (PVE) may enhance the proven efficiency of TACE in patients with unresectable HCC. We herein report the case of a 56-year-old cirrhotic woman with a voluminous HCC unsuitable for surgical resection. Yet, complete tumour necrosis and prolonged survival could be achieved after a combined porto-arterial embolization. This case emphasizes the potential synergistic effect of a combined arterio-portal embolization and the hypothetical survival benefit of such a procedure, in selected patients, with HCC not suitable for surgery or local ablative therapy.

INTRODUCTION

Despite a close observation of patients with liver cirrhosis, hepatocellular carcinoma (HCC) is often diagnosed at an advanced stage where no optimal treatment has been established[1-3] only few patients (20%-25%) will benefit of resection or liver transplantation[4], only chance to improve life expectancy. Actually, 80% to 90%[5] of HCC develop in cirrhotic patients with impaired liver function, limiting the possibility of safe major liver resections. If liver resection has shown a survival benefit, in case of cirrhosis, it's a risky procedure with a high prevalence of postoperative liver failure and should not be performed if the future liver remnant (FLR) is estimated to be less than 40%[6]. In those patients who are not suitable for surgery, treatment is palliative and survival is poor and correlated to TNM stage (TNM classification of primary liver cancer by the International Hepato-Pancreato-Biliary Association[7]) and liver damage severity[8]. Despite previous inconclusive randomized controlled trials comparing transarterial chemoembolization (TACE) to conservative treatment in unresectable HCC[9-11], Liovet *et al*[12] ultimately demonstrated that TACE led to an increased survival in selected patients with preserved liver function. TACE is now widely accepted as the procedure of choice in selected patients who are not eligible for

resection or local ablative therapy. However, the question remains whether combined portal embolization may enhance the proven efficiency of TACE in patients with unresectable hepatocellular carcinoma (HCC).

We herein report the case of a cirrhotic patient with advanced HCC in whom complete tumour necrosis and prolonged survival were observed following a combined porto-arterial embolization.

CASE REPORT

A 56-year-old woman with alcoholic cirrhosis, Child-Pugh A6 presented with an 80 mm HCC stage Ⅲ. The tumor developed in the right hepatic lobe, impinging on the median hepatic vein and in contact with the right glissonian pedicle (Figure 1A). There were two satellite nodules but the left hepatic lobe was free of tumor. The right portal vein was patent. The patient had stopped alcohol intake for 3 mo before admission. There was no past history of encephalopathy, ascites or upper gastro-intestinal bleeding despite stage I oesophageal varices. The clinical examination was normal. Liver biochemistry showed: A 74% prothrombin time, normal albumin level, bilirubin 50 μmol/L (N < 17), ASAT/ALAT: 59/66 UI/L (N < 40), gamma glutamyl transferase: 204 UI/L (N < 140), alkaline phosphatase: 105 UI/L (N < 80), platelet count was 126 000/mm^3. Alpha-foeto protein level was 108 μg/L (N < 5). The diagnosis of established alcoholic cirrhosis was confirmed by a percutaneous liver biopsy. As the surgical strategy was a right hepatectomy removing the median hepatic vein and the patient underwent a right portal vein embolization (PVE) prior to surgery (Figure 2A and B). After 4 wk the left lobe had gained 40%. During surgery, intra-abdominal exploration revealed moderate to severe portal hypertension with an enlarged spleen, mild ascites and dilated splanchnic veins. The liver appeared cirrhotic with regeneration nodules. Intraoperative ultrasound confirmed an 8 cm HCC, mainly involving segment V and Ⅷ, invading the median hepatic vein and close to the right glissonian pedicle. Peroperative observation precluded liver resection and separate biopsy of both tumor and liver parenchyma was done before abdominal closure. In view of previous right PVE, intra-arterial chemoembolization was thought to be unsafe and a supportive medical care was decided. During follow-up, a 20 mm intra-tumoral aneurysm of right arterial branch was diagnosed on computer tomography (CT) scan (Figure 1B), most probably related to an arterial trauma during intraoperative tumor biopsy. A supra-selective arterial embolization with coils was then undertaken with complete obliteration of the arterial aneurysm on control angiography (Figure 3A and B). A control CT scan performed 3 mo later showed complete necrosis of the tumor (Figure 1C) as suggested by return of alpha-foeto protein to normal value (6.8 μg/L). Disease-free survival lasted for two years. Multiple intra-hepatic and bone recurrence was diagnosed on progressive increase of alpha foeto-protein level. The patient ultimately died after a follow-up of three years.

DISCUSSION

In up to 90%, HCC develop in cirrhotic patients whose impaired liver function precludes major liver resections if FLR is less than 40%[6]. First reported by Makuuchi *et al*[13], PVE can be performed safely[14] in order to induce a homolateral liver parenchyma atrophy and a hypertrophy of the FLR, allowing resection in patients with large tumors or abnormal liver function[15]. Yet, this technique was initially described for patients with Klatskin tumors[13] and its' application to cirrhotic patients with HCC is debated by some authors who rather recommend a preoperative combined arterio-portal embolization[16]. HCC being hypervascular tumours mainly fed by an arterial blood flow, cessation of the portal's flow leads to a compensatory increased flow in the corresponding arterial territory[17] that may cause the tumor progress.

Recently, Ogata *et al* [18] have reported in a controlled trial the feasibility and efficacy of a sequential arterio-portal embolization, TACE followed by PVE after a 3 wk delay, before major liver resection in cirrhotic patients with HCC. When compared to PVE alone, this procedure offers a significantly higher rate of complete tumor necrosis (83% *vs* 5%, P < 0.001), a higher 5-year disease-free survival rate (37% *vs* 19%, P = 0.041) with a similar rate of morbidity. In this report the authors confirmed that complete tumor necrosis can be obtained by its complete blood flow privation (arterial and portal) and highlight the potential benefit of this sequence in term of prognosis. Moreover, in their report, the Beaujon's group[18] suggests that sequential embolization could effectively be an appropriate treatment itself in patients in whom surgery is precluded due to a poor degree of liver hypertrophy.

In case of unresectable HCC, efficacy of TACE is now admitted[19,20] with a benefit in survival when compared to conservative treatment. Yet, TACE alone leads to around 50% of complete tumour necrosis[21-23] whereas this rate is over 80% after sequential arterio-portal embolization and this may have an impact on survival curves[16,18]. Aoki *et al*[16] obtained a necrosis rate superior to 70% in 12/17 (71%) whereas Yamakada *et al*[24] observed a complete tumoral necrosis in 7/9 (78%) of the resected specimen after a sequential arterio-portal procedure with 1, 3 and 5 years survival rates of 87%, 72% and 51%, respectively.

Even though portal vein thrombosis, which is a frequent complication of HCC, is considered to be an absolute contraindication to TACE, due to increased risk of post procedure liver failure or infarction, efficacy and safety of TACE in such cases have been reported[25] in selected patients. Taken together, these observations suggest a good tolerance of liver parenchyma to ischemia when interval between portal and arterial occlusion is delayed[18]. Ogata *et al*[18] who have suggested a minimum of 3 wk between both procedures had lesser morbidity and aminotransferase levels as compared to Aoki *et al*[16] who performed both embolizations within a period of 7 d.

In the case herein reported, although our patient

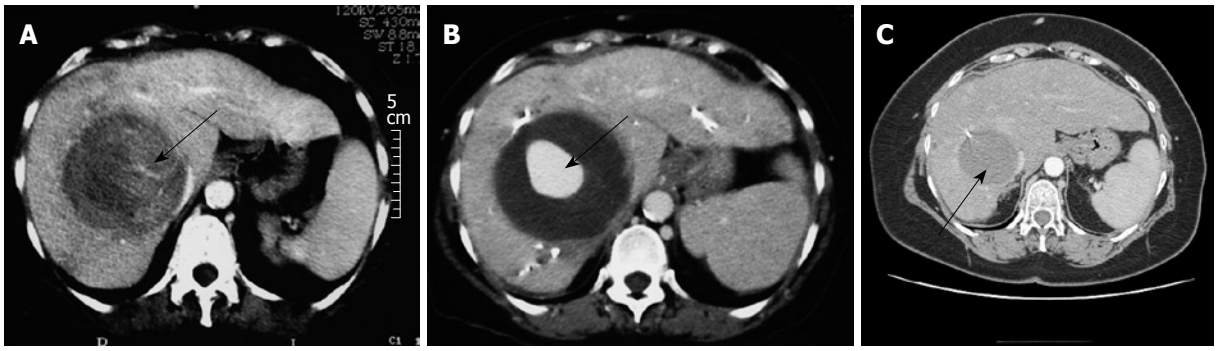

Figure 1 Enhanced CT scan. A: Showing an eighty millimetre HCC (black arrow) developed in the right hepatic lobe, driving back the median hepatic vein, in contact with the right glissonian pedicle; B: Showing an arterial aneurysm (black arrow) due to the main tumour artery traumatism during biopsy; C: Showing complete tumour necrosis after combined portoarterial embolization (black arrow).

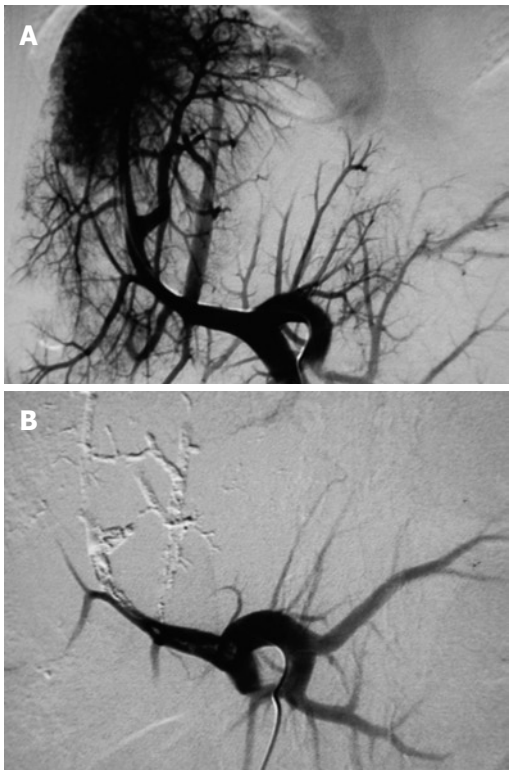

Figure 2 Portography. A: Prior to embolization; B: After embolization.

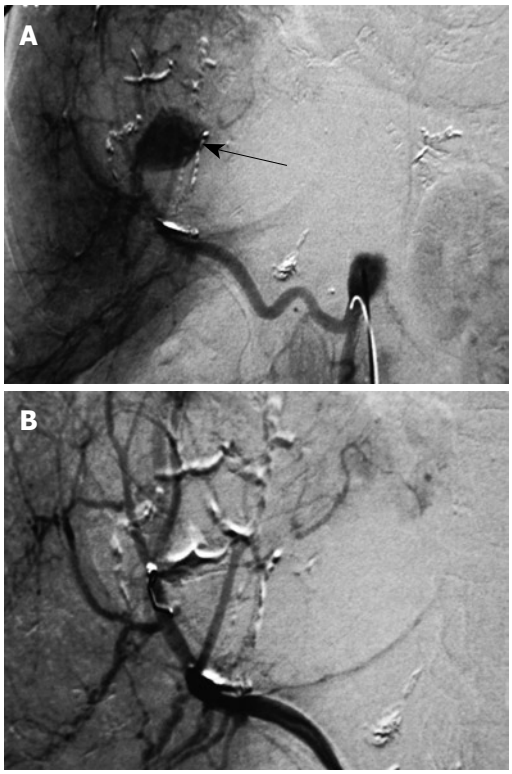

Figure 3 Arteriography. A: The arterial aneurysm developed on the HCC main feeding artery (black arrow), prior to embolization with coils; B: After complete arterial occlusion with coils.

was planned to have a major liver resection we did not perform a preoperative TACE before PVE, which is now systematic in our department. In this particular case, arterial embolization was performed after portal embolization and was indicated to treat a traumatic arterial aneurysm following a peroperative fine needle biopsy. Yet, it was well tolerated, had no consequence on liver function and led to a complete tumor necrosis with a prolonged survival. We agree that a porto-arterial sequence is unusual and do not recommend it that way, but this case fully illustrates the synergy of a combined embolization in term of tumor necrosis. We rather recommend a sequential arterio-portal sequence combining TACE and PVE as previously described[18], with a 3 wk delay between both procedures. In this view, we assume that tolerance is related to the sequence and its timing whereas efficacy is related to both, arterial and portal, HCC vascular exclusion.

Our report aims at giving further support to the combination of TACE and portal embolization in the treatment of voluminous HCC that cannot be treated by surgery or alternative therapy such as radiofrequency as previously hypothesized by others[18]. We assume that cirrhotic liver parenchyma has a relatively good tolerance to arterial and portal ischemia when the interval between both vascular occlusions is delayed (at least 3 wk). Proven efficacy of TACE might be enhanced by a combined sequential PVE. Patients With large HCC, not suitable for surgery or local ablative therapy, could effectively be treated with combined arterio-portal embolization with a limited morbidity and a likely benefit in survival.

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