A CASE OF HEPATIC TUMOR IN WHICH AN ENHANCING CAVITY APPEARED DURING TRANSCATHETER ARTERIAL CHEMOEMBOLIZATION

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(received 21 February 2011, accepted 13 May 2011)

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Abstract

We encountered a case of hepatic tumor in which an enhancing cavity became evident during transcatheter arterial chemoembolization (TACE). The imaging findings of the tumor on ultrasonography and computed tomography were typical of hepatocellular carcinoma (HCC). During TACE, a well-defined, enhancing cavity appeared unexpectedly in the tumor, and pseudoaneurysm was suspected. As the cavity did not embolize well using additional epirubicin-iodized oil emulsion and porous gelatin particles, more definitive embolization was performed using microcoils to avoid adverse events, such as intratumoral bleeding or rupture of the pseudoaneurysm. Microcoils were placed both distal and proximal to the cavity in the feeding artery, and hepatic angiography after this procedure revealed disappearance of both tumor stain and the cavity.

Key words : hepatocellular carcinoma (HCC), transcatheter arterial chemoembolization (TACE), microcoil embolization, peliotic change

Introduction

Adverse events can be associated with transcatheter arterial chemoembolization (TACE), such as intratumoral hemorrhage during the procedure[1)] or intraheptic aneurysm formation after the procedure[2)]. Although embolic agents, such as gelatin sponge particles and iodized oil, have been speculated as the cause of such events, determining the definite cause of such phenomena seems difficult. Appearance of an unexpected intrahepatic structure in connection with TACE is a common feature in previously reported cases and the present case.

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Case report

A 68-year-old man was incidentally diagnosed with hepatic dysfunction while consulting a local doctor for investigation of upper airway symptoms in 1998. He remained under intermittent follow-up. In June 2009, abdominal ultrasonography demonstrated a tumor in segment 7 of the right lobe of the liver. The inner structure of the lesion showed a mosaic pattern, surrounded by a halo-like area of low echogenicity. The patient was referred to our hospital for further investigation. Precontrast computed tomography (CT) showed a hypodense tumor, approximately 4 cm in diameter (Fig. 1a), in the same region as on ultrasonography. Dynamic CT showed features typical of hepatocellular carcinoma (Fig. 1b, c), as well as the findings previously seen on ultrasonography. Hepatocellular carcinoma was diagnosed based on imaging findings and TACE was planned. In

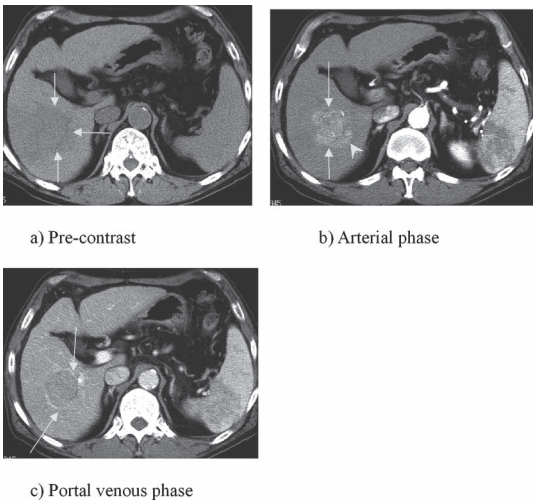


Fig. 1. Dynamic CT. Pre-contrast CT (a) demonstrates a hypodense area in the right lobe of the liver (arrows). Arterial phase (b) shows dense enhancement of the tumor (arrows) with extension into the posterior branch of the right portal vein (arrowhead). Portal phase (c) shows wash-out of contrast material from the tumor and peripheral rim enhancement (arrows).

August 2009, he was admitted to our hospital for TACE. He had no history of transfusion. Serum levels of alpha-fetoprotein (AFP) and protein induced by vitamin K antagonist II (PIVKA II) were within normal limits. Child-Pugh class was A. Negative results were obtained for hepatitis B surface antigen and anti-hepatitis C antibody, and other laboratory data were unremarkable. The mid-arterial phase of celiac arteriography showed a stain in the right lobe of the liver, consistent with the hepatic tumor detected on ultrasonography and CT. A small tumor stain thought to represent a satellite nodule was also apparent in the right lobe of the liver (Fig. 2). The portal phase of superior mesenteric arteriography revealed encasement of the posterior branch of the right portal vein. To perform TACE, a microcatheter with a 2.1-Fr tip (Tangent ; Boston Scientific Japan, Tokyo, Japan) was inserted into the main feeding artery. The catheter system including a 4.2-Fr catheter (SHK Kanazawa™ ; Hanaco Medical, Saitama, Japan) and the microcatheter were heparinized throughout the procedure, using 1,000 units of heparin sodium (Novo heparin™ ; Mochida Pharmaceutical, Tokyo, Japan) dissolved in 500 mL of saline. Selective arteriography performed via the main feeding artery of the tumor showed a round tumor stain (Fig. 3). The contrast solution consisted of 10 mg of epirubicin hydrochloride (Farmorubicin™ ; Pfizer Japan, Tokyo, Japan) dissolved in 1 mL of contrast material comprising iopamidol (Iopamiron 370™ ; Bayer Schering Pharma, Tokyo, Japan), emulsified with 1 mL of iodized oil (Lipiodol Ultra-Fluid™ ; Guerbet Japan, Tokyo, Japan). The

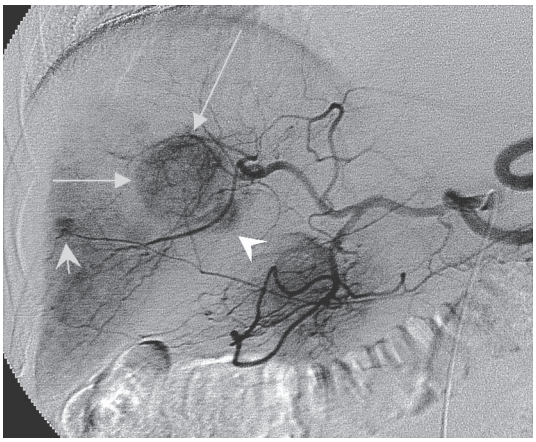


Fig. 2. Mid-arterial phase of celiac arteriography shows the main tumor stain (arrows) and a satellite nodule (short arrow) in the liver. The main tumor extends inferomedially (white arrowhead).

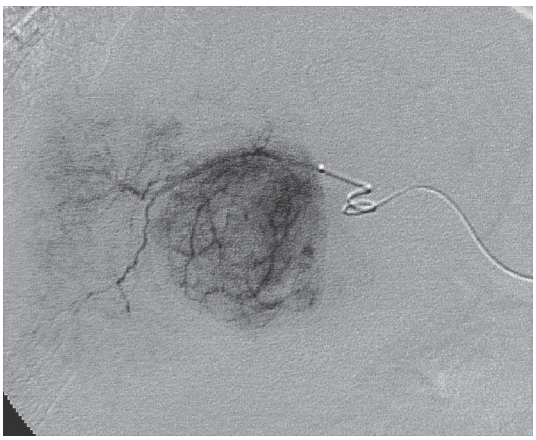


Fig. 3. Selective arteriography performed via the main feeding artery of the tumor shows a round tumor stain.

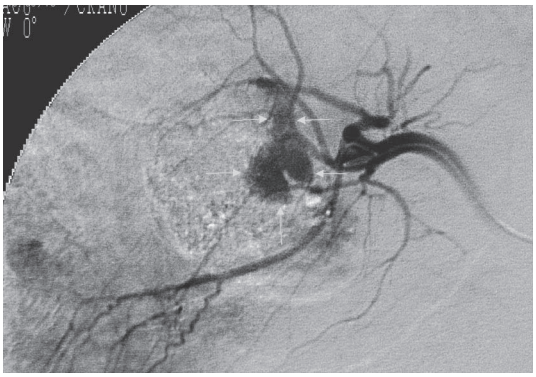
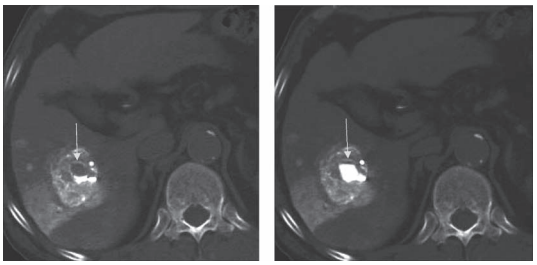


Fig. 4. A well-circumscribed enhancing cavity appears unexpectedly in the tumor after injection of porous gelatin particles (arrows).



a) b)

Fig. 5. CT arteriography via the feeding artery. On precontrast CT, the cavity in the tumor contains iodized oil in the dorsal region, and the unembolized ventral portion (a, arrow) can be seen. This portion shows overt contrast enhancement after injection of contrast solution via the feeding artery (b, arrow).

total volume of this emulsion was injected into the main feeding artery. A mixture of porous gelatin particles (Gelpart™ ; Astellas Pharma, Tokyo, Japan) and the contrast material was then injected into the main feeding artery. The same emulsion mentioned above was then prepared again, and the total volume was delivered into another feeding artery, followed by embolization using porous gelatin particles. Arteriography performed after this embolization showed the unexpected appearance of a well-circumscribed enhancing cavity (Fig. 4). This was not accompanied by any change in vital signs, which remained stable throughout the procedure. The enhancing cavity was also seen in bilateral anterior oblique projections, and thus appeared to lie within the tumor. The

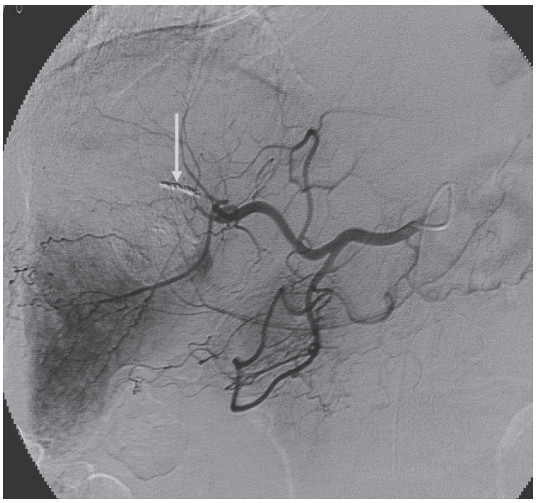


Fig. 6. Common hepatic arteriography after TACE reveals disappearance of all tumor stains. The red arrow indicates microcoils.

cavity resembled a region of peliotic change associated with HCC, and we therefore prepared more emulsion containing 14 mg of epirubicin and 1.4 mL of iodized oil. This emulsion was injected into the cavity, and further embolization was conducted using porous gelatin particles. To confirm the effect of this embolization, we performed CT arteriography via the feeding artery. Although this demonstrated accumulation of iodized oil in part of the intratumoral cavity, the rest of the cavity contained no iodized oil and instead showed overt contrast enhancement, suggesting an unembolized portion (Fig. 5). Angiography after CT arteriography demonstrated gradual wash-out of the emulsion and porous gelatin particles from the cavity. Another method of embolization was therefore considered necessary, and the microcoil method was selected. Using two 2 mm × 4 cm microcoils (Interlocking Detachable Coil™ ; Boston Scientific Cork, Cork, Ireland), further arterial embolization was performed both distal and proximal to the cavity. Common hepatic arteriography was conducted to evaluate embolization, revealing that all stains, including the residual stain, had disappeared (Fig. 6). CT performed 1 week after embolization showed good accumulation of iodized oil in the tumor. However, CT performed 4 months after the embolization revealed enhancement

suggesting recurrence at the bottom of the tumor. Recurrence of the satellite nodule was also observed. A second session of TACE was therefore performed, during which we confirmed that the main tumor had different feeding arteries from those observed in the first procedure. Epirubicin-iodized oil emulsion and porous gelatin particles were injected into the arteries. Abundant accumulation of iodized oil in the tumors was demonstrated on follow-up CT.

Discussion

In the present case, the hepatic tumors were consistent with HCC in terms of imaging findings and clinical course. During TACE, a well-circumscribed, homogeneous stain suggestive of a cavity-like structure in the main tumor was identified. This could have been a necrotic cavity or cavernous structure known as peliosis hepatis[3,4] or peliotic change[5], a term used to refer to the formation of blood-filled cavities in a liver tumor, particularly HCC. The structure might also have been a vessel-derived structure, such as pseudoaneurysm. CT performed before TACE did not show any finding that suggested the presence of this kind of spatial structure in the tumor, and the finding appeared for the first time after injection of porous gelatin particles.

Some previous published articles have reported the occurrence of adverse events concerning TAE/TACE of HCCs (Table 1). Choi *et al*. reported intratumoral hemorrhage during TACE[1]. Aso *et al*. described formation of multiple intrahepatic pseudoaneurysms following TACE[2]. Battula *et al*.[6], Sakamoto *et al*.[7], Pijl *et al*.[8] and Nakao *et al*.[9] reported tumor rupture after TACE. Choi *et al*. speculated that the cause of the adverse event was embolic agents, such as antineoplastic agents, iodized oil, and gelatin sponge particles[1]. Aso *et al*. suggested io-

Table 1. Reports of adverse events concerning TAE/TACE of HCC

	Authors	Age/sex	Adverse events	Underlying disease	TA(C)E	Intervention or operation for AE	Outcomes
1	Battula *et al*.[6] (2007)	(1) 61M	tumor rupture after TACE	liver cirrhosis	DOX+IO	surgical debridement	died within 48 h
		(2) 69M	tumor rupture after TACE	liver cirrhosis	DOX+IO	none	alive after over 6 months
2	Choi *et al*.[1] (2004)	64M	intratumoral hemorrhage during TACE	HBV(+), No LC?	MMC+IO+ GSP	microcoil embolization	coil embolization was effective
3	Sakamoto *et al*.[7] (1999)	65F	tumor rupture after TAE	HBV(+), iver cirrhosis	IO	TAE (ineffective)+ segmentectomy	discharged 3 weeks after operation
4	Pijl *et al*.[8] (1999)	59F	tumor rupture after TACE	n.p. (for liver) duodenal ulcer existed	DOX+IO+ GSP	surgery (s/o rupture of duodenum due to ulcer)	died 3 days after TACE
5	Nakao *et al*.[9] (1988)	57M	tumor rupture after TAE	liver cirrhosis	GSP	not performed	died 7 days after intraabdomimal hemorrhage
6	Aso *et al*.[2] (1994)	(1) 63F	MIHPAn after TACE	chr. hepatitis	MMC+IO+ GSP	none	no rupture of PAn
		(2) 64M	MIHPAn after TAE	liver cirrhosis	IO+ GSP	none	no rupture of PAn
		(3) 55M	MIHPAn after TACE	chr. hepatitis	MMC+IO+ GSP	none	no rupture of PAn
		(4) 58M	MIHPAn after TACE	liver cirrhosis	MMC+IO+ GSP	none	no rupture of PAn
		(5) 61M	MIHPAn after TACE	chr. hepatitis	MMC+IO+ GSP	none	no rupture of PAn

Abbreviations
AE, adverse event ; chr., chronic ; DOX, doxorubicin ;
GSP, gelatin sponge particles ;
HBV, hepatitis B virus ; IO, iodized oil ; LC, liver cirrhosis ;
MIHPAn, multiple intrahepatic pseudoaneurysms ;
MMC, mitomycin C ;
PAn, pseudoaneurysm ; s/o, suspected of.

dized oil, gelatin sponge particles, or both as the cause of the adverse event[2]. Battula *et al*. speculated that rupture following TACE might be due to tumor and capsular necrosis with secondary infection or vascular injury resulting from the TACE procedure or chemotherapeutic agents used in TACE[6]. Similarly, in the present case, embolic materials including epirubicin hydrochloride, iodized oil, and gelatin sponge particles might have been related to appearance of the cavity in the tumor. However, the contents and combinations of embolic materials used in the reports shown in Table 1 varied, so identifying which materials represent the main causes of events is likely to prove difficult, as it was in the present case. The intratumoral cavity that appeared in the present case might be a necrotic cavity, or another kind of structure known as peliosis hepatis. This histological term defines a condition characterized by multiple small cystic blood-filled spaces in the liver[3]. Peliosis hepatis reportedly occurs predominantly in people dying of tuberculosis[3]. HIV infection is reportedly associated with hepatic sinusoidal abnormalities, including peliosis hepatis[10]. Wakabayashi *et al*. suggested an association of peliosis hepatis with anabolic steroid therapy[11]. Hoshimoto et al. described the finding of HCC with extensive dilated sinusoid-like structures, or peliotic changes[5]. They speculated that this change was caused by increased sinusoidal pressure and impaired outflow of blood from the tumor because of immaturity of the sinusoid-like structures and central lobular veins in the cancer nodule[5]. Whether the present case represented peliotic change is unclear. Nonetheless, the cavernous structure we encountered might have been present in the main tumor before TACE, and might have become apparent during the procedure due to effects such as increased intratumoral pressure when the embolic materials were injected. In addition, some function of embolic materials including anticancer drug, iodized oil, and gelatin sponge particles might have been involved in the appearance of the intratumoral cavity. However, as pathological data were not obtained in the present case, the mechanisms underlying the formation of this cavernous structure remain obscure. Despite repeated attempts at embolization using both emulsion and porous gelatin particles, the cavity did not embolize well, and the embolic agents appeared mobile within. The tumor might have contained pathways through which embolic agents flowed away from the cavity, but this was not able to be confirmed. The injected embolic agents were thus thought not to be useful. The presence of a residual cavity was considered to indicate insufficient chemoembolization of the tumor, suggesting a risk of recurrence, as well as occurrence of adverse events such as intratumoral hemorrhage or intrahepatic pseudoaneurysm formation. The true nature of the cavity remained unclear. However, whatever the observed cavity was, taking the safest measures to avoid any possible adverse events was considered necessary, as some people have died of adverse events resulting from TACE for HCC (Table 1). Performing embolization of the feeding artery as completely as possible was considered important to prevent tumor recurrence. We therefore considered the performance of more definitive embolization as warranted. Thus, we performed selective arterial coil embolization both distal and proximal to the cavity, trapping the cavity between the two embolized arterial portions and isolating it completely from the blood flow of the feeding artery. Complete embolization of the feeding artery might make transarterial approaches to this region of the artery difficult in the case of recurrence. However, we regarded prevention of adverse events as the most important consideration. No adverse events have occurred since the first TACE, and we noted no recurrent lesions fed by the same artery. In conclusion, we encountered a case of hepatic tumor that was clinically diagnosed as HCC, showing an enhancing cavity within the tumor during TACE. Although we eventually selected microcoil embolization, further accumulation of studies appears essential for determining the optimal course of action in such cases.

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