Cerebral lipiodol embolism related to a vascular lake during chemoembolization in hepatocellular carcinoma: A case report and review of the literature

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Abstract
A male patient underwent conventional transcatheter chemoembolization for advanced recurrent hepatocellular carcinoma (HCC). Even after the injection of 7 mL of lipiodol followed by gelatin sponge particles, the flow of feeding arteries did not slow down. A repeat angiography revealed a newly developed vascular lake draining into systemic veins; however, embolization was continued without taking noticing of the vascular lake. The patient’s level of consciousness deteriorated immediately after the procedure, and non-contrast computed tomography revealed pulmonary and cerebral lipiodol embolisms. The patient’s level of consciousness gradually improved after 8 wk in intensive care. In this
artery (LHA), and the postprocedural course was undergone TACE for the same lesion for 3 years. Eight months prior to admission, he had a second TACE. He had a history of type-B cirrhosis to the left diaphragm was admitted to our hospital for most of the lateral segment of the liver and expanding.

CASE REPORT

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INTRODUCTION

Transcatheter arterial chemoembolization (TACE) is utilized worldwide for the treatment of patients with unresectable hepatocellular carcinoma (HCC). Although various complications of TACE have been reported[1], cerebral lipiodol embolism (CLE) after TACE is very rare. To our knowledge, 27 cases have been reported in the English literature, and possible pathways for carrying lipiodol from HCCs to systemic arteries have been hypothesized[2-18]. This is the first report of CLE, in which a vascular lake emerged during conventional chemoembolization, draining into systemic veins and causing pulmonary and cerebral lipiodol embolism.

Key words: Transcatheter arterial chemoembolization; Arteriovenous shunt; Hepatocellular carcinoma; Vascular lake; Cerebral embolism

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Core tip: Vascular lakes that resemble extravasation within hepatocellular carcinomas occasionally emerge during chemoembolization. To date, the drainage routes from vascular lakes are not well understood. We present a patient with a recurrent large hepatocellular carcinoma in which a vascular lake emerged during conventional chemoembolization, draining into systemic veins and causing pulmonary and cerebral lipiodol embolism.

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DISCUSSION

TACE has been widely accepted as an effective therapy for HCC. Lipiodol is the most common embolic material used in TACE; it is usually mixed with anticancer drugs dissolved in non-ionic contrast medium. Lipiodol can enter the microcirculation of the tumor and flow into the surrounding portal vein, which is the main drainage route from the hypervascular HCC[19]. However, lipiodol
TACE via IPA frequently results in pulmonary complications due to the existence of an AV shunt between the IPA and PA\(^{[25]}\). Some authors speculated that communication between the IPA and pulmonary vessels via adhesive pleurae or tumor invasion is the most likely pathway from the tumor to the PA\(^{[4,6]}\). In the present case, we performed IPA embolization using glue under DSA guidance, and the glue fragment never flowed into the pulmonary vessels.

In most previously reported cases of CLE, including the case described herein, a large dose of lipiodol was infused (Table 1). Cerebral and pulmonary lipiodol embolisms have been reported in patients receiving more than 20 mL of iodized oil after TACE of HCC\(^{[4,6,14,16,18]}\). According to Kishi et al\(^{[26]}\), when lipiodol was infused into the dog’s hepatic artery, the amount of lipiodol oil deposition in the lungs was proportional to the lipiodol dose infused. They also found lipiodol deposits in the brain and pancreas\(^{[26]}\). These findings suggested a dose-dependent circulation of oil droplets via hepatic sinusoids to pulmonary capillaries and then into the systemic circulation. It was suggested that the lipiodol dose should not exceed 15-20 mL to prevent the risk of an extrapulmonary embolism\(^{[4,6]}\). Nevertheless, in 7 previous cases, CLE occurred when the lipiodol dose was < 15 mL\(^{[2,5,7,14,18]}\). The required lipiodol dose was determined by multiple factors, including the blood supply to the tumor, tumor size, catheter position and liver function reserve. When lipiodol goes through an intratumoral AV shunt, the dose of lipiodol required to accomplish HCC flow stasis increases. If there had not been an intratumoral AV shunt in the presented case, we could have accomplished flow stoppage with a lower dose of lipiodol.

CLE is thought to be associated with intrapulmonary or intracardiac shunts\(^{[4,7,10,16]}\). Evidence of an underlying intracardiac right-to-left shunt was proven by transesophageal echocardiogram in one previous case\(^{[27]}\); however, the pathway from the PA to the LA was not verified in most previously reported cases of CLE, including the present case. Wu et al\(^{[26]}\) speculated that an intra-pulmonary arteriovenous shunt might appear during pulmonary lipiodol embolization due to increasing pulmonary artery pressure or hypoxia. Wu et al\(^{[10]}\) added that communication between the systemic and pulmonary vessels might develop via adhesive pleurae or tumor invasion of the diaphragm, leading to a right-to-left shunt. In a case report of delayed CLE, Wu et al\(^{[26]}\) concluded that the rapid flow of the feeding artery washed out the lipiodol, and the lipiodol deposited in the lungs was washed out again upon entering the systemic circulation. Since it has been verified that fat globules < 7 \(\mu\)m in diameter can pass directly through the pulmonary arteriolar network\(^{[26]}\), lipiodol can enter the systemic circulation in the absence of a right-to-left shunt to cause cerebrovascular complications.

In summary, we presented a case in which a vascular lake draining into systemic veins caused a lipiodol cerebral embolism. As intratumoral AV shunts via vas-
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Figure 2 Infused 140 mg of miriplatin suspended in 7 mL of lipiodol via the left hepatic artery. A: Left hepatic angiography shows a large hypervascular tumor in the left hepatic lobe and intrahepatic metastases neighborhood without an intratumoral AV shunt; B: Repeated left hepatic angiography shows a vascular lake in the superior portion of the tumor (arrow) that developed after chemoembolization; C: Venous phase shows drainage into the pericardiocophrenic vein (arrow heads), which was unrecognized until remasking and pixel shifting were performed. AV: Arteriovenous.

because the pathways from the PA to the LA cannot be blocked regardless of the mechanism by which they are developed.

ARTICLE HIGHLIGHTS

Case characteristics
A 63-year-old man with a large hepatocellular carcinoma underwent transcatheter arterial chemoembolization (TACE), but his level of consciousness deteriorated immediately after the procedure.

Clinical diagnosis
CT scan of the brain revealed multiple lesions of increased attenuation, and cerebral lipiodol embolism (CLE) was confirmed.

Differential diagnosis
There is no differential diagnosis.

Laboratory diagnosis
No specific finding was obtained by laboratory testing.

Imaging diagnosis
An angiography during TACE procedure revealed a newly developed vascular lake draining into systemic veins, which offered a pathway carrying lipiodol to pulmonary vessels and was the most likely cause of this serious complication.

Pathological diagnosis
No pathological examination was performed.

Treatment
The patient was treated in our intensive care unit.

Related reports
This is the first report of CLE, in which vascular lake phenomenon emerging during the procedure caused intratumoral arteriovenous shunt and played the most important role for its occurrence.

Term explanation
The term CLE describes cerebral lipiodol embolism.

Experiences and lessons
Arteriovenous shunt via vascular lake may develop during chemoembolization, repeated angiography during TACE procedures should be performed to prevent
CLE, especially when it is difficult to obtain a decrease of blood flow.

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