Pulmonary lipiodol embolism after transcatheter arterial chemoembolization for hepatocellular carcinoma

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DECLARATIONS

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Key Message

Pulmonary lipiodol embolism is a fatal but preventable complication of transcatheter arterial chemoembolization.

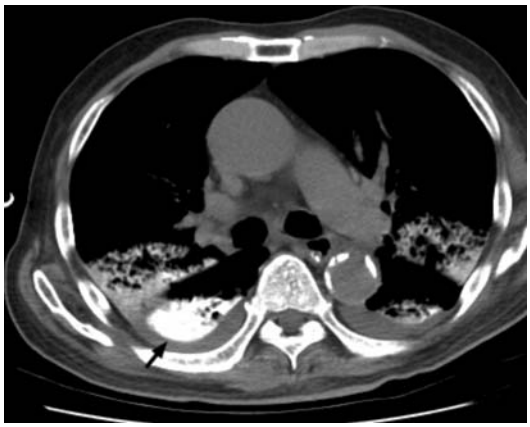
Introduction

Transcatheter arterial chemoembolization (TACE) has become an effective alternative treatment strategy for patients with inoperable hepatocellular carcinoma (HCC). Although TACE is relatively safe, pulmonary lipiodol embolism is a rare and potentially fatal complication which is often not anticipated by physicians.[1] About 14 patients with pulmonary lipiodol embolism progressing to respiratory distress were reported in previous literature. Here, we report a patient with HCC who survived a severe pulmonary lipiodol embolism requiring mechanical ventilatory support and uneventfully received the second course of TACE. In this article, we sum previous literature and have discussed the possible pathophysiological mechanism underlying this complication and risk factors for its development.

Case history

A 76-year-old man, weighing 65 kgs and an alcoholic drinker who consumed at least 500 mL of whiskey per day, was diagnosed with a hepatic tumor by abdominal sonography during a routine health check-up. A triphasic helical computed tomography (CT) scan revealed this hepatic tumor to be 14.5 × 8.1 cm in size over segments 4, 7 and 8, with global enhancement in the hepatic arterial (HA) phase and contrast washout in the portal venous (PV) phase. His serum α-fetal protein level was 9.57 ng/mL. Angiography of the celiac, common hepatic, and superior mesenteric arteries showed prominent arteriovenous (AV) shunting due to early venous drainage into the middle hepatic vein and the right atrium. TACE was performed for this inoperable HCC via the right and left hepatic arteries. A total of lipiodol 40 mL, adriamycin 40 mg, and Gelfoam fine particles were injected. Unfortunately, the patient felt dyspneic immediately after TACE and his oxygen saturation recorded by pulse oximetry (SpO_2) fell to 90% despite the use of a non-rebreathing mask. A chest radiograph showed diffuse bilateral air-space consolidations with a normal heart size. Within 30 minutes, he was intubated due to severe hypoxic respiratory failure. His PaO_2/FiO_2 ratio was 53.3 and serum D-dimer level 15.64 μg/mL. His right internal jugular venous pressure was below 6 mmHg. Chest CT without contrast enhancement revealed retention of radiopaque lipiodol not only within the hepatic tumor, but also in the dependent portions of both lungs, especially on the right lower lung lobe (Figure 1). He underwent mechanical ventilation with a protective ventilatory strategy. Methylprednisolone 40 mg was administered every six hours. The lower molecular weight heparin (LMWH), enoxaparin, was given at a dose of 1 mg/kg for a total of two days. His PaO_2/FiO_2 ratio improved dramatically to more than 250 within two days and was liberated from mechanical ventilation at post-TACE day 5. The follow-up chest radiograph revealed complete resolution of the bilateral pulmonary infiltrates in three weeks. He underwent TACE again 27 days after the first course using the same injection

Figure 1
Chest CT scan after TACE without contrast enhancement revealed high-density lipiodol deposition in the dependent part of the bilateral upper and lower lung field (arrow)



routes but at a reduced dose of lipiodol (10 mL). Before injection, the AV shunt was still present but the bypass flow was less prominent than that shown in the previous angiograph. The procedure was uneventful. He was discharged home in a stable condition and continued to be followed up at our outpatient clinic.

Discussion

Pulmonary lipiodol embolism, first reported by Samejima *et al.* in 1990,[2] is attributed to pulmonary arterial occlusion by iodized oil, which is injected into the hepatic artery and bypassed into the lungs through the normal hepatic vasculature or through an AV shunt. Although 23% of asymptomatic patients had abnormalities on pulmonary perfusion scans after TACE,[3] the development of respiratory symptoms is uncommon. The incidence of symptomatic pulmonary lipiodol embolism after TACE ranged between 0.05–1.8%.[1,4] These results confirmed the speculation that most pulmonary complications of TACE improve or resolve spontaneously.

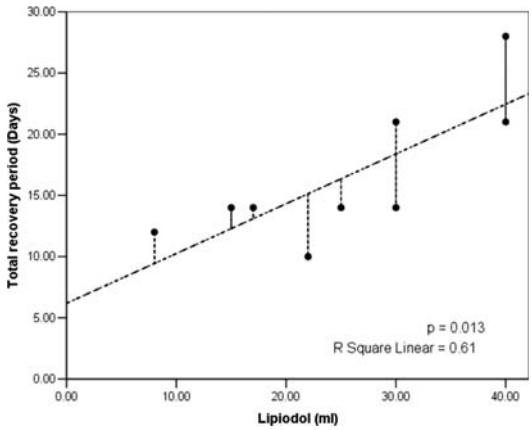
The most likely mechanism of symptomatic pulmonary injury is a high concentration of unbound free fatty acids resulting from breakdown of oil microemboli, which might lead to pulmonary capillary leakage and non-cardiogenic pulmonary oedema.[4] A summary of the case

Table 1
Summary of previous case reports for pulmonary lipiodol embolism after TACE in patients with primary liver cancer

Reference	*Patient No./ Sex/Age (years)*	*Cancer type*	*Maximal tumor size (cm)*	*TACE Method*		*Period of symptom onset (days)*	*Total recovery period (days)*	*Outcome*
				LO (ml)	*C/T* (mg)*			
1	1/NM/NM	PLC	NM	25	NM	0.5	–	E
2	2/M/75	HCC	NM	8	40	0.04	12	S
4	3/M/44	HCC	17	40	60	4	28	S
4	4/M/56	HCC	18	30	50	5	14	S
4	5/F/31	HCC	20	30	50	2	21	S
4	6/M/61	HCC	18	26	50	4	–	E
4	7/M/57	HCC	20	25	55	2	14	S
4	8/M/55	HCC	14	22	50	2	10	S
10	9/NM/NM	Hepatoblastoma	NM	14	NM	0	NM	NM
11	10/M/27	HCC	10	10	8	4	–	E
11	11/M/63	HCC	15	17	13	1	14	S
12	12/F/81	HCC	14	15	NM	4	14	S
13	13/F/7	HCC	11	10	NM	0.04	–	E
Our patient	14/M/76	HCC	14	40	40	0	21	S

NM = no mentioned in articles, TACE = transcatheter arterial chemoembolization, E = expired, S = survival, M = male, F = female, HCC = hepatocellular carcinoma, PLC = primary liver cancer, LO = lipiodol, C/T = chemotherapy
*Chemotherapy includes adriamycin, cisplatin, or doxorubicin hydrochloride

Figure 2
A positive correlation of the amount of injected lipiodol and total radiological recovery period in survived patients of primary liver cancer, developing pulmonary lipiodol embolism after TACE ($r = 0.78$, $p = 0.013$)



reports published in literature is shown in Table 1. Among patients who survived these episodes, there was a significant correlation ($r = 0.78$, $p = 0.013$), between the amount of lipiodol injected and the duration of patient recovery, which is an indicator of the severity of lung injury (Figure 2).

A number of risk factors for pulmonary lipiodol embolism after TACE including the dose of iodized oil injected, the presence of an AV shunt, and trans-inferior phrenic artery (IPA) embolization.[4,5] Among these factors, the amount of iodized oil injected was the most important, especially when more than 20 mL of iodized oil was used.[4] In our case, the secondary course of TACE was uneventful after reducing the dose of lipiodol and existing a smaller AV shunting.

As for reducing the degree of AV shunting, successful experience by temporary balloon occlusion of hepatic vein branch with AV shunts[6] in HCC patients with marked AV shunting was published. Embolization of AV shunting with polyvinyl alcohol, gelatine sponges, or coils may be an alternative strategy.[7,8] However, if AV shunting is refractory and severe after above-mentioned strategies, TACE is contraindicated.

Similar to fat embolism syndrome, no therapy has been shown to be effective for pulmonary lipiodol embolism. Anecdotal success has been achieved with treatments including oxygenation, high-dose methylprednisolone, heparin, and positive end-expiratory pressure (PEEP).[9] In this patient, his oxygenation responded dramatically after using a protective ventilatory strategy, methylprednisolone, and LMWH. Corticosteroids can limit local accumulation of free fatty acids, inhibit complement-mediated leukocyte aggregation, and block further cytokine storm. LMWH is beneficial in counteracting blood cell aggregation to prevent further arterial occlusion. These managements may facilitate recovery of such fulminant pulmonary lipiodol embolism with ARDS.

In conclusion, pulmonary lipiodol embolism can be a serious complication after TACE. Risk factors of this complication may include the dose of iodized oil injected, the presence of AV shunting, and trans-IPA embolization. There is a significant correlation between the amount of lipiodol and clinical severity of pulmonary injury. Our experience from this case suggests that this complication could be prevented by limiting the dose of lipiodol injected and by reducing the degree of AV shunting. Our treatment strategies may also provide insights into optimal management of this life-threatening complication.

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