

# Cerebral lipiodol embolism during transcatheter arterial chemoembolization

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**Abstract**—Cerebral lipiodol embolism (CLE) is a rare complication that may occur during chemoembolization. The authors present three cases of CLE during transcatheter arterial chemoembolization for hepatocellular carcinoma. Multiple small nonconfluent hyperintense intracerebral lesions were found on the diffusion-weighted and fluid-attenuated inversion recovery MRI. Clinical signs completely resolved and MRI lesions markedly improved on follow-up evaluation within a 3-week period.

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Recent development of advanced hepatocellular carcinoma treatment includes use of mixture of lipiodol (an oily contrast medium) and chemotherapeutic agent, which is then injected into the feeding artery near the tumor site.<sup>1</sup> Before injection, lipiodol is mixed with the anticancer drug forming a stable covalent conjugate; this mixture is then slowly injected. Documented complications of transcatheter arterial chemoembolization (TACE) include pulmonary embolism; however, cerebral complications have not been reported.<sup>2</sup>

We recently encountered three cases of cerebral lipiodol embolism (CLE). Neurologic signs were nonspecific, and MRI showed multiple small nonconfluent hyperintense signal changes on diffusion-weighted and fluid-attenuated inversion recovery (FLAIR) MRI.

**Case reports.** *Patient 1.* A man aged 52 years with advanced hepatocellular carcinoma underwent a second course of TACE at the hepatic artery via right femoral artery puncture using a mixture of 35 mL lipiodol and 100 mg Pharmorubicin (Pharmacia S.p.A., Milan, Italy) (an anthracycline derivative). During the procedure he had headache, followed by confusion and left upper extremity weakness. Blood pressure was 130/80 mm Hg during and after the procedure. There was no breathing difficulty, and skin examination was normal without petechial rash. Arterial blood gas analysis showed a PaO<sub>2</sub> of 74.7 mm Hg, consistent with mild hypoxia. Initial CT was unremarkable; 4 days later, MRI showed multiple discrete high signal lesions in the gray-white matter junction, both thalamus, cerebral, and cerebellar hemispheres on T2-weighted, FLAIR, and diffusion-weighted images (figure 1, A through C). There was no hyperintense lesion on T1-weighted image. Three weeks later, a follow-up MRI showed marked resolution (figure 1D). Subsequent evaluation to look for intracardiac shunt was unrevealing without evidence of shunt on transthoracic and transesophageal echocardiograms. His neurologic symptoms recovered completely when discharged 3 weeks later.

*Patient 2.* A man aged 58 years with hepatocellular carcinoma underwent TACE using a mixture of 8 mL lipiodol and 100 mg epirubicin hydrochloride. During the procedure he had visual loss. Two hours later, he noted mild shortness of breath, frontal and occipital headache, and chest pain. Blood pressure was 120/80

mm Hg during the procedure and 130/80 mm Hg after the procedure. Arterial blood gas analysis at this time showed mild hypoxemia with a PaO<sub>2</sub> of 70.2 mm Hg. Examination was consistent with cortical blindness without retinal lesions. The same day MRI revealed multiple, discrete, high signal lesions in the gray-white matter junction and right cerebellum on FLAIR and diffusion-weighted images (figure 2, A and B). There was no hyperintense lesion on T1-weighted image. Three weeks later, a follow-up MRI revealed near complete resolution of the lesions. His vision quickly returned to baseline over several days. Transthoracic and transesophageal echocardiograms were unremarkable without evidence of shunt.

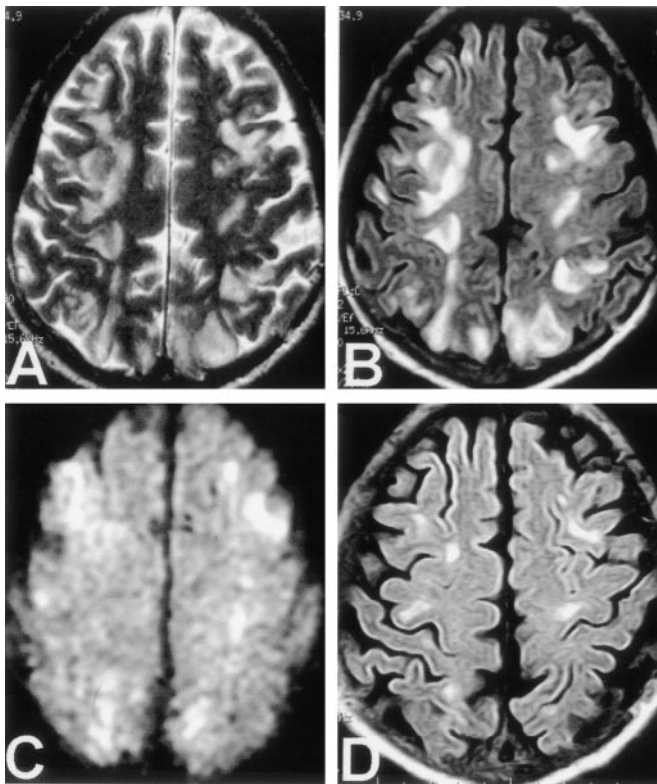
*Patient 3.* A man aged 56 years with hepatocellular carcinoma underwent a third course of TACE. During the procedure he had disorientation, irritability, and blindness. Eleven hours later, brain MRI demonstrated diffuse, multiple high signal lesions in the white matter and cerebellar hemispheres on FLAIR and diffusion-weighted images (figure 2, C and D). There was no hyperintense lesion on T1-weighted image. He noted tachypnea, and arterial blood gas analysis showed a PaO<sub>2</sub> of 66 mm Hg. Blood pressure was 140/90 mm Hg during the procedure and 130/80 mm Hg after the procedure. Two weeks later, his neurologic symptoms recovered completely.

**Discussion.** Various complications have been reported with TACE; however, CLE has not been reported to the best of our knowledge.<sup>2</sup> Overall clinical and MRI findings in our cases resemble arterial fat emboli after traumatic long bone fractures.<sup>3</sup> Fat emboli typically start with respiratory symptoms caused by pulmonary arterial showering, and then neurologic symptoms follow. Elevated pulmonary arterial pressure subsequently results in cardiac or pulmonary shunt, and cerebral fat emboli from bone marrow may result. Common neurologic manifestations include nonspecific encephalopathy with minor focal findings, and even transient cortical blindness may occur.<sup>4,5</sup> MRI appearance in all of our cases was strikingly similar, and all cleared rapidly. Although similar lesions have been reported with either hypotension (watershed ischemia)<sup>6</sup> or hypertension (hypertensive encephalopathy),<sup>7</sup> review of medical records show no significant variation on blood pressure. Serum creatinine and blood urea nitro-

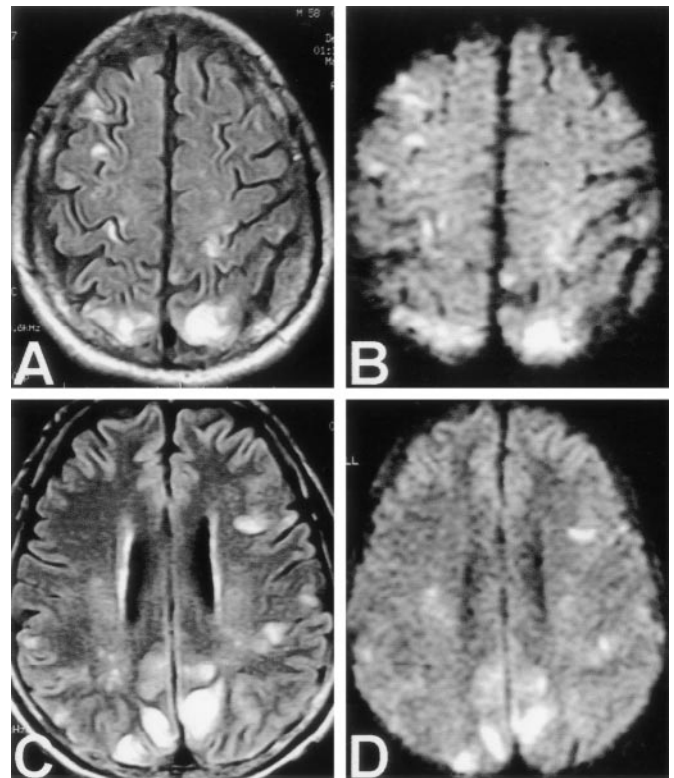
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**Figure 1.** Axial T2-weighted (A), fluid-attenuated inversion recovery (FLAIR; B) and diffusion-weighted (C) MRIs obtained on day 4, and follow-up FLAIR (D) image obtained 3 weeks after the transcatheter arterial chemoembolization in Patient 1. The initial images (A, B, and C) show multiple, hyperintense lesions near the gray-white matter junction of both hemispheres. Follow-up image (D) reveals marked resolution.



**Figure 2.** MRIs (A, B) obtained 26 hours after the transcatheter arterial chemoembolization in Patient 2 and MRIs (C, D) obtained 11 hours after the transcatheter arterial chemoembolization in Patient 3. Axial fluid-attenuated inversion recovery (FLAIR; A) and diffusion-weighted (B) images show multiple, hyperintense lesions on both hemispheres. Axial FLAIR (C) and diffusion-weighted (D) MRIs show similar appearance.

gen levels at the event were normal. Some chemotherapeutic drug use has been known to give similar MRI appearance.<sup>7,8</sup> Usually these cases have seizures with unremarkable DWI. Thus far, Pharmorubicin has not been implicated.

All of our patients had evidence of pulmonary involvement but without demonstrable intracardiac shunt. It has been shown fat globules <7  $\mu\text{m}$  in diameter can pass directly through the pulmonary arteriolar network (i.e., transpulmonary shunt) and result in cerebral injury.<sup>9</sup> Therefore, presence of intracardiac shunt may not be necessary as has been demonstrated in mongrel dogs.<sup>10</sup>

Although we were able to demonstrate multiple ischemic lesions primarily near the gray-white matter junction, none of the lesions showed diagnostic lipid density expected from lipiodol. Resulting lesions most likely reflect secondary vasogenic and cytotoxic ischemic changes from lipiodol emboli.<sup>3</sup> The small size of the lipid droplets that occluded distal vessels was overshadowed by adjacent larger ischemic changes.

However, MRI findings in our patients look similar to those of posterior leukoencephalopathy syn-

drome; no significant blood pressure variation and renal insufficiency, association of TACE, evidence of pulmonary involvement on the lung perfusion-diffusion scans (Patients 1 and 2), and multiple focal perfusion defects on the hexamethylpropylene amine oxime SPECT (Patient 1) could be important findings suggesting a diagnosis of CLE.

Our cases, collected during a 10-year period from a single institution, suggest lipiodol emboli may be rare. Symptoms may be nonspecific, and spontaneous recovery with supportive therapy can be expected. MRI, especially diffusion-weighted imaging, seems to be a useful indicator for the diagnosis of CLE. To reduce the risk of lipiodol embolism, a smaller lipiodol dose and survey for detection of intracardiac shunt before the procedure can be considered.

## References

1. Nakamura H, Hashimoto T, Oi H, Sawada S. Transcatheter oily chemoembolization of hepatocellular carcinoma. *Radiology* 1989;170:783-786.
2. Sakamoto I, Aso N, Nagaoki K, et al. Complications associated with transcatheter arterial embolization for hepatic tumors. *Radiographics* 1998;18:605-619.

3. Parizel PM, Demey HE, Veeckmans G, et al. Early diagnosis of cerebral fat embolism syndrome by diffusion-weighted MRI (starfield pattern). *Stroke* 2001;32:2942–2944.
4. Jacobson DM, Terrence CF, Reinmuth OM. The neurologic manifestations of fat embolism. *Neurology* 1986;36:847–851.
5. Kusumoto S, Imamura A, Watanabe K. Case report: the incidental lipid embolization to the brain and kidney after lymphography in a patient with malignant lymphoma: CT findings. *Clin Radiol* 1991;44:279–280.
6. Wityk RJ, Goldsborough MA, Hillis A, et al. Diffusion- and perfusion-weighted brain magnetic resonance imaging in patients with neurologic complications after cardiac surgery. *Arch Neurol* 2001;58:571–576.
7. Hinchey J, Chaves C, Appignani B, et al. A reversible posterior leukoencephalopathy syndrome. *N Engl J Med* 1996;334:494–500.
8. Edwards MJJ, Walker R, Vinnicombe S, Barlow C, MacCallum P, Foran JM. Reversible posterior leukoencephalopathy syndrome following CHOP chemotherapy for diffuse large B-cell lymphoma. *Ann Oncol* 2001;12:1327–1329.
9. Sevitt S. The significance and pathology of fat embolism. *Ann Clin Res* 1977;9:173–180.
10. Byrick RJ, Mullen JB, Mazer CD, Guest CB. Transpulmonary systemic fat embolism. Studies in mongrel dogs after cemented arthroplasty. *Am J Respir Crit Care Med* 1994;150:1416–1422.

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