Neurological Sciences (2019) 40:1959–1961
https://doi.org/10.1007/s10072-019-03854-y

LETTER TO THE EDITOR

Cerebral lipiodol embolism after transarterial hepatic chemoembolization studied with susceptibility-weighted imaging

Marta De Simone[1] · Barbara Brogna[2]

Received: 4 January 2019 / Accepted: 15 March 2019 / Published online: 23 March 2019

Dear Editor,

Cerebral lipiodol embolization (CLE) is a rare but potential complication associated with chemoembolization procedures such as transarterial embolization/chemoembolization (TAE/TACE) and interventional lymphatic procedures (ILP). Predisposing factors are hepato-pulmonary, pulmonary arteriovenous, or right-to-left intracardiac shunts. CLE is potential neurologic morbidity, and it usually displays typical neuroimaging patterns on computed tomography (CT) and magnetic resonance imaging (MRI). According to previous studies, CLE is characterized by disseminated lesions across multiple vascular territories, mainly at the distal gray matter [1]. However, lipiodol's chemical proprieties have been poorly investigated.

A 79-year-old man affected by multifocal hepatocarcinoma (HCC) with a vascular invasion of the left branch of the portal vein underwent a second course of TACE via the proper hepatic artery by using a mixture of 10 mL lipiodol, 25 mg pirarubicin, and gelatin sponge particles (900 μm) and coils (5 mm × 8 mm). The liver function was ranked A in the Child-Pugh classification system, and his alpha-fetoprotein (AFP) was 140 μg/L. About 24 h after the procedure, the patient appeared in a confusional state and aphasic.

A routine blood examination showed the hemoglobin value (Hb) at 10.9 g/dL, the white blood cell count at 9800/mm^3, and the platelet count at 78.000/mm^3. The blood pressure was 130/80 mmHg and the pulse rate, the respiratory rate, and the body temperature were normal.

The neurological examination showed a lower facial nerve palsy and a mild right-sided hemiparesis (muscle scale grades MRC 4/5). No neurological pathological reflex was observed. A brain CT without contrast was immediately performed to rule out a stroke. The CT scan showed high-attenuating areas in the right frontal sulci (Fig. 1a) and hyperdense spots in the left parietal sulcus. Other multiple foci of hypodense ischemic areas were also seen in the cerebellum (Fig. 1b). Suspecting a CLE, an MRI was requested 48 h later. All sequences were performed on a 1.5 T Magnetom Aera, Siemens-Germany. The diffusion-weighted imaging (DWI) revealed multiple foci ischemic areas in the cerebral cortex (Fig. 1c), basal ganglia, thalami, and cerebellum. The corresponding lesions showed low signal areas on the ADC map and hyperintensities on the T2 weighted images and fluid attenuation inversion recovery (FLAIR) sequences as ischemic areas in the subacute phases (Fig. 1d). The SWI confirmed that in the right frontal sulci (Fig. 2a, b, c) and in the left parietal sulcus which are the areas of susceptibility and highlighted two other areas in the left caudate body (Fig. 2d, e, f) and left periventricular white matter (Fig. 2g, h, i). In the filtered imaging phase, a negative shift that resembled lipiodol depositions were visible (Fig. 2b, e, h). The patient was followed-up regularly with hematological, microbiological, and biochemistry examinations. His neurological status gradually improved under adequate hydration and supportive therapies.

A follow-up head CT obtained 5 weeks after the second TACE showed no abnormality, and the previously observed lipiodol deposition had entirely cleared up.

Discussion

The lipiodol neurotoxicity mechanism still remains unknown, but it could be related to its vaso-occlusive, lipid, osmolar, chemical, or physical properties [2]. As an iodinated contrast agent, lipiodol may potentially penetrate or cause the breakdown of the blood-brain barrier and extravasate into the neural

✉ Marta De Simone
martadesimone@gmail.com

[1] Neuroradiology Unit, "San Giuseppe Moscati" Hospital Avellino, Amoretta Street, 83100 Avellino, Italy

[2] Institution of Radiology at 'University of Study of Campania, Luigi Vanvitelli', piazza Miraglia 2, 80138 Naples, Italy

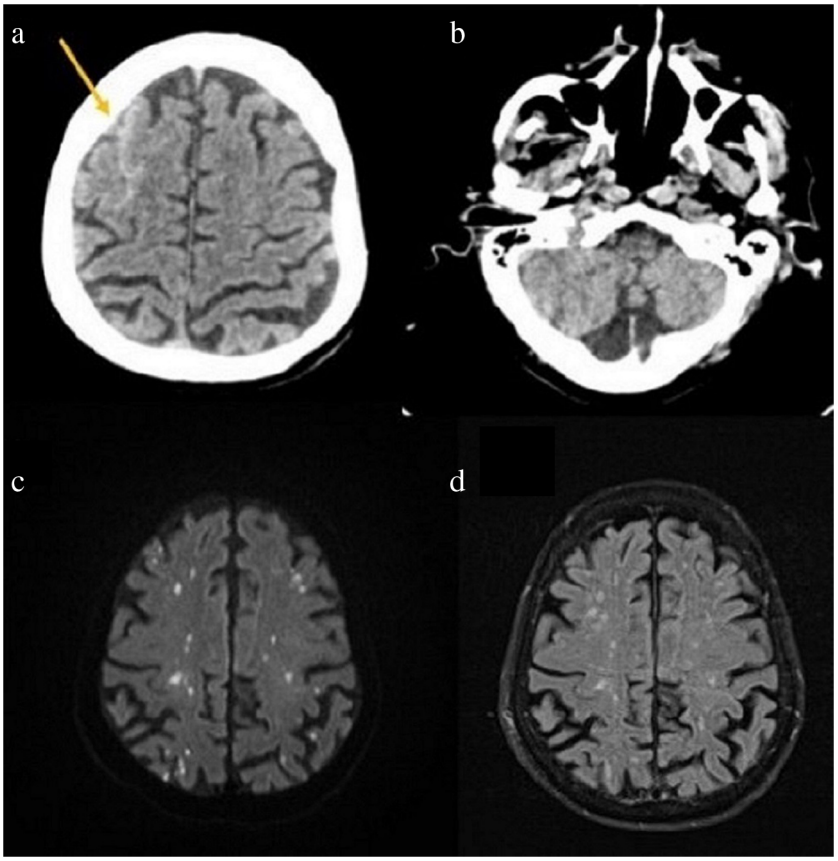

Fig. 1 Head non-contrast CT showed high attenuation areas in the right frontal sulci (yellow arrow) (**a**) and some hypodense foci in the cerebellum (**b**); Diffusion-weighted imaging (**c**) and T2 fluid attenuation inversion recovery (FLAIR) (**d**) of head MRI showed multiple and disseminated hyperintensity/high signal lesions at the cerebral hemispheres corresponded to multiple ischemic areas in the subacute phase

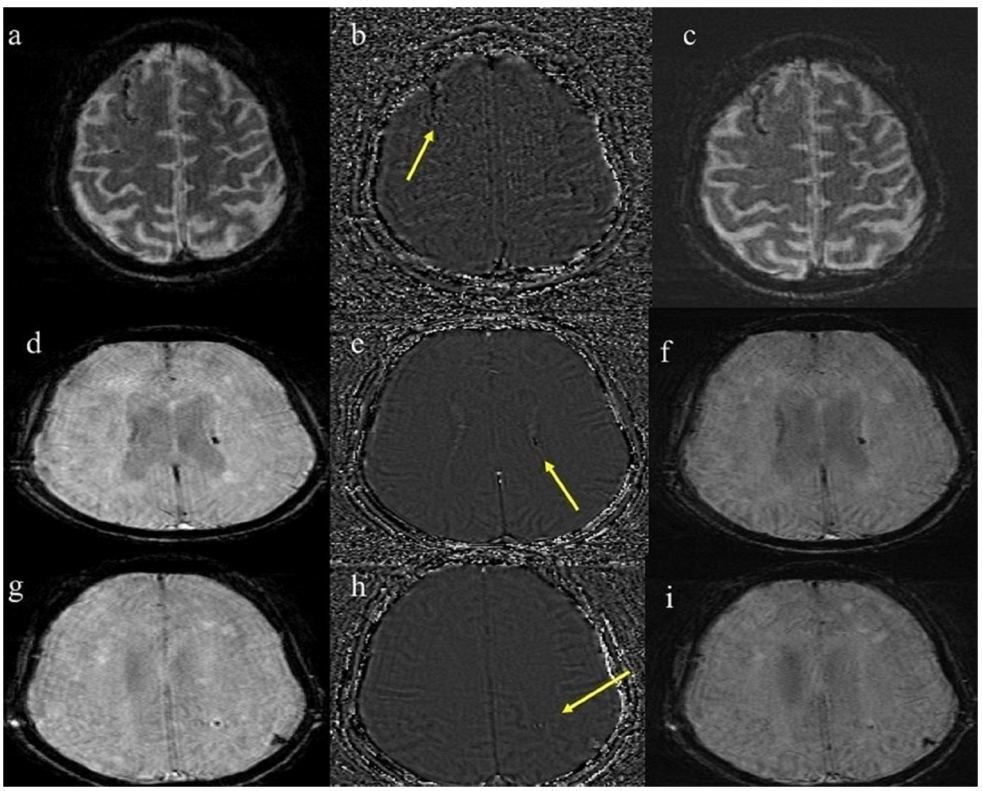

Fig. 2 In these figures, SWI images with magnitude image (first image), phase-filtered images (second image) and SWI (third image) in each line is described. The right frontal sulcus appeared dark on magnitude (**a**) and SWI image (**c**) with negative shift (**b**) on the phase image. The SWI highlighted the other two areas that were not visible on CT scan in the left caudate body and in the periventricular white matter with the same characteristics. Magnitude image (**d**) and SWI image (**f**) in the left caudate body with negative shift (**e**) and magnitude image (**g**), SWI image (**i**) and phase image (**h**) in the left periventricular white matter. Yellow arrows indicate the corresponded negative shift in the phase image

tissue, causing direct toxicity and eliciting local cytotoxic and vasogenic edema. Risk factors of CLE are multiple embolization procedures due to the better surveillance, the amount of lipiodol used, and the existence of arteriovenous shunts. Hepatic arterio-pulmonary vein shunts are associated with pulmonary vein invasion of HCC and can be found in patients with advanced HCC. In theory, embolization material may pass from the hepatic artery into the hepatic vein via aberrant connections created by an HCC invasion. Chung et al. (1993) [3] recommended that clinicians should not use more than 20 mL of lipiodol during TACE to prevent a pulmonary oil embolism. In our case, a total of 20 ml lipiodol was given in two TACE sessions.

An intracardiac right-to-left shunt via a patent foramen ovale or an intrapulmonary arteriovenous shunt can also lead to CLE. Pulmonary arteriovenous (AV) shunts are usually hereditary but can also be observed in a number of acquired conditions including trauma and metastatic disease. Literature has reported about 30 cases of CLE in the last 20 years. All cases were associated with TAE/TACE procedures and the only two developed during interventional lymphatic procedures.

The site of lipiodol deposition includes the basal ganglia, thalamus, gray-white matter conjunction, and both parietal and frontal cortices. CLE usually appears on head CT images with multiple hyperdense areas. It has been hypothesized that these high attenuation areas correspond to lipiodol depositions, even though the coexistence of microhemorrhagic foci have not been excluded. The dual-energy CT proved that the hyperdensities were lipiodol rather than just multifocal hemorrhage [4].

Usually, on head MRI, multiple areas of acute cerebral ischemic change that have decreased water diffusion in infarcted tissue, increased signals in DWI, and decreased ADC signals are visible. Larger areas of hyperintensities on FLAIR rather than on DWI for the same lesions indicate the existence of peri-stroke edema [1]. These features suggest a possible component of small vessel/capillary occlusive disease from the lipiodol. On an MRI, CLE needs to be differentiated from other etiologies such as hypoperfusion-related ischemia, cerebral embolism including cerebral fat embolism, and posterior reversible encephalopathy syndrome.

SWI is a novel MRI technique that exploits the magnetic susceptibility differences of various tissues, such as blood, iron, and calcification. SWI is based on high-resolution, three dimensional (3D), full velocity-compensated gradient echo sequences using both magnitude and phase images.

The phase images are useful in differentiating between diamagnetic and paramagnetic susceptibility effects of calcium and blood, respectively. However, colors of blood and calcium on SWI phase images are scanner-dependent [5]. Siemens uses so-called "left-handed" reference schemes where blood products appear bright and calcium or diamagnetic substance appear dark. A more recent study (Kirshen et al. 2016) [2] about CLE that used SWI described the lesions as microhemorragic foci. In our case, the hyperdensity areas on the CT showed a negative shift in the phase image, and they appeared dark. These features may suggest that areas of depositions of quantities of sluggish lipiodol have a diamagnetic effect like calcium. This data corresponds with imaging features of a dual energy CT.

In conclusion, SWI proved the lipiodol diamagnetic effect. This feature suggests that neurotoxicity mechanisms can also lead to its chemical propriety.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from the patient.

References

1. Yoo KM, Yoo BG, Kim KS, Lee SU, Han BH (2004) Cerebral lipiodol embolism during transcatheter arterial chemoembolization. Neurology 63(1):181–183
2. Kirschen MP, Dori Y, Itkin M, Licht DJ, Ichord R, Vossough A (2016) Cerebral lipiodol embolism after lymphatic embolization for plastic bronchitis. J Pediatr 176:200–203
3. Chung JW, Park JH, Im JG, Han JK, Han MC (1993) Pulmonary oil embolism after transcatheter oily chemoembolization of hepatocellular carcinoma. Radiology 187:689–693
4. Lee CS, Kim SJ, Choi JW, Choi CG, Lee DH (2010) Cerebral lipiodol embolism proven by dual-energy computed tomography: a case report. J Computer Assist Tomogr 34(1):105–106
5. Halefoglu AM, Yousem DM (2018) Susceptibility weighted imaging: clinical applications and future directions. World J Radiol 10(4): 30–45