Delayed cerebral lipiodol embolism after transcatheter arterial chemoembolization of hepatocellular carcinoma

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Transcatheter arterial chemoembolization (TACE) has been an effective mean in treating hepatocellular carcinoma for nearly 30 years. The reported complications associated with TACE mainly include acute hepatic failure (accounting for 0.26%), liver abscess (0.22%), multiple intrahepatic aneurysms (0.17%), hepatic artery occlusion (1.52%), spontaneous rupture of tumor (0.15%), gallbladder infarction (0.3%), perforation of duodenum (0.05%), acute renal failure (0.05%), pulmonary embolism (0.17%), femoral nerve injury (0.15%), etc.1,2 Cerebral lipiodol embolism is a rare complication of TACE. To our knowledge, only 6 cases of cerebral lipiodol embolism after TACE were previously reported,3-6 all of which occurred during or immediately after TACE. The delayed cerebral lipiodol embolism has not been reported. In this article, we reported a case of cerebral lipiodol embolism that occurred 69 hours after TACE of hepatocellular carcinoma and discussed the mechanism and measures of prevention.

CASE REPORT

A 51-year-old woman who complained of upper-abdominal distention for 45 days and fever for 15 days was admitted to our hospital. B-ultrasonography and CT for upper-abdomen revealed a huge tumor in the right liver (segments V and VI). The concentration of blood AFP was 1185.3 ng/ml. HBsAg was positive, while hepatic function was classified as A according to Child-Pugh classification. The patient was diagnosed as chronic hepatitis B, hepatocirrhosis and massive hepatocellular carcinoma in the right liver. The first TACE was performed in December, 2004. As revealed by angiography, the huge hypervascular tumor located in the right liver was only supplied by the right hepatic artery (RHA) without arteriovenous shunt. TACE was performed via the RHA using a mixture of 40 mg pirarubicin, 40 ml lipiodol, 20 mg hydroxycamptothecine and 150 mg Oxaliplatin. Toward the end of the procedure, the lipiodol was deposited in the tumor densely. The patient recovered quickly and was discharged 10 days after TACE. Four weeks later, a follow-up CT showed that lipiodol was deposited sparsely in the tumor. So the second TACE was performed. During the second procedure, the finding of angiography was similar to the previous one (Figure 1). A mixture of 40 mg pirarubicin, 40 ml lipiodol, 20 mg hydroxycamptothecine and 150 mg Oxaliplatin was infused via the RHA. The embolism process was monitored by fluoroscopy all the way and no abnormal flow of the lipiodol was found. Postoperative abdominal X-ray plain film showed a dense lipiodol deposition in the tumor and the patient did not feel any discomfort during the procedure. Thirty-four hours after the second TACE, the patient had chest distress and dyspnea suddenly, with SPO2 decreasing from 98% to 85%. Emergency chest radiograph showed high density in left lower lung field, suggesting pulmonary lipiodol embolism. Through adding O2 and injecting 10 mg dexamethasone, the corresponding symptoms alleviated. Sixty-nine hours after the second TACE, the patient had chest distress and dyspnea again, then experienced headache, dizziness, asthenia and transient unconsciousness. Thoracic CT obtained 5 hours later demonstrated that hyper-attenuating lipiodol deposited in the bilateral basal lungs (Figure 2). A noncontrast head CT showed generally increased attenuation in bilateral pallium, basal nuclei, and thalamencephalon (Figure 3). The pulmonary and cerebral lipiodol embolism was considered. One week later, all nervous symptoms of the patient disappeared after the intervention of active dehydration, diuresis and nutrition of nerve, and the patient was discharged.

Five weeks later, the patient had a return visit. Hepatic CT showed a sparse lipiodol deposition in the right hepatic tumor (Figure 4A), which suggested that the patient required the third TACE. Considering that no obvious arteriovenous shunt in two previous hepatic angiographies was found, and pulmonary and cerebral embolism occurred 34 hours and 69 hours after TACE respectively, pulmonary and cerebral embolism might be caused by the lipiodol washed out from the tumor resulting from quicker blood flow of tumor feeding artery. If the blood flow of tumor feeding artery was slowed down effectively after TACE, pulmonary and cerebral embolism might be avoided. Thus, we used coils (vortex-18 coil, Boston scientific, USA) to embolize...
partly the feeding artery of tumor for reducing the flow of the vessel (Figure 5) after dense deposition of lipiodol in the tumor during the third TACE procedure. After the operation, chest distress, dyspnea and nervous symptoms did not occur. Seven days later, plain thoracic and abdominal CT showed no obvious pulmonary lipiodol embolism and dense lipiodol deposition in the tumor. The cranial CT showed no abnormality and the previously observed lipiodol deposition had been cleared entirely. Four weeks later, follow-up liver CT showed dense lipiodol deposited in the tumor (Figure 4B). So far, the patient still lives healthily.

**DISCUSSION**

Cerebral lipiodol embolism rarely occurs after TACE for hepatocellular carcinoma. And there are only 6 reported cases of patients who developed cerebral lipiodol embolism during or immediately after the TACE. In these reports, only two of them were analyzed for possible mechanism. Wu et al.\(^5\) thought that pulmonary and cerebral lipiodol embolism was possibly correlated closely with the bypass between tumor feeding artery and pulmonary vessels owing to tumor invading the thoracic cavity. Matsumoto et al.\(^6\) concluded that communication between tumor feeding artery and pulmonary vein might have occurred via adhesive pleural or tumor invasion into the diaphragm. Therefore, small dose of lipiodol could enter systemic circulation quickly and caused cerebral embolism. In the present case, pulmonary and cerebral lipiodol embolism occurred 34 and 69 hours after TACE respectively. Since the tumor was located in segments V and VI and was far away from the diaphragm, its blood was only fed by the RHA, there was no bypass as mentioned above. The repeated hepatic angiography did not reveal any arteriovenous shunt. Second, the tumor was huge and hypervascular, the blood flow of tumor feeding artery was fast. Third, the patient presented with symptoms of respiratory system 34 hours after TACE. Chest radiograph revealed pulmonary lipiodol embolism. Forth, nervous symptoms emerged 35 hours after the respiratory system symptoms, which suggested that cerebral embolism occurred after the pulmonary embolism. According to the features mentioned above, lipiodol was washed out from the tumor by faster blood flow of tumor feeding artery, resulting in pulmonary embolism. Then lipiodol deposited in the lung was washed out again and entered systemic circulation,
leading to cerebral embolism. Therefore, during the third TACE, we used coils to embolize part of tumor feeding artery to reduce its blood flow after the lipiodol was deposited in the tumor densely.

The mechanism of cerebral lipiodol embolism is similar to that of cerebral fat embolism. Microscopically, fat embolism are observed mainly in the gray matter because of it abundant capillary network. In this case, the noncontrast head CT showed that generally increased attenuation in bilateral pallium, basal nuclei, and thalamencephalon, which reflected the pathologic features. So the CT finding of multiple focal area of increased attenuation in gray matter region is characteristic for cerebral lipiodol embolism according to the history of TACE for hepatocellular carcinoma.

REFERENCES


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