

Answering Reviewers

Name of journal: World Journal of Gastroenterology

Manuscript NO: 40670

Title: **Cerebral lipiodol embolism related to a vascular lake during chemoembolization: A case report and review of the literature**

Thank you very much for your review of our manuscript. We have made corrections and additions to our manuscript in response to the comments and instructions of Reviewers. Our incorporation of the reviewers' suggestions is as follows :

#### **Reviewer's comment (Reviewer's code 03656580)**

Authors reported a case in which a vascular lake draining into systemic veins caused a lipiodol cerebral embolism. As intratumoral AV shunts via vascular lakes may develop during chemoembolization, performing repeated angiography during TACE procedures, especially when obtaining a decreased blood flow is difficult. When an intratumoral AV shunt is identified by angiography, embolization of the feeding artery using coils or glue should be considered instead of an additional injection of lipiodol or embolic particles. They developed a method to prevent lipiodol accumulation in the lungs because the pathways from the PA to the LA cannot be blocked regardless of the mechanism.

#### **Response to reviewer 03656580**

Thank you very much for your review of our manuscript.

#### **Reviewer's comment (Reviewer's code 00039518)**

This case report is well written and shows that the formation of intratumoral vascular lake during chemoembolization for hepatocellular carcinoma may be the cause of pulmonary and cerebral lipiodol embolism which are rare but serious complications of this therapeutic procedure. I only think that the Authors should better specify which was the segment of the left lobe in which the treated tumor was placed and the location within the liver of the other multiple intrahepatic metastases

#### **Response to reviewer 03656580**

Thank you very much for your review of our manuscript.

We have made corrections and additions to our manuscript in the CASE REPORT on page 5, line 11.

A 63-year-old man with a large recurrent HCC replacing most of the lateral segment of the liver and expanding to the left diaphragm was admitted to our hospital for a second TACE.

#### Reviewer's comment (Reviewer's code 02439215)

#1. The tumor artery hepatic venous shunt is considered to be an important cause of the formation of cerebral lipiodol embolism (CLE), while the adjacent or invasion of the diaphragm and the bottom of the lungs, the phrenic artery and the blood supply, the rich blood supply of the tumor, the right to left shunt in the heart, and the large amount of iodide oil in the operation are the risk factors for the cerebral lipiodol embolism (CLE). The article should also analyze whether these factors lead to cerebral lipiodol embolism in this case.

#2. The introduction should be followed by an explanation of why the case report is novel or merits review. This expression can be more obvious.

#3. There should be enough detail for the reader to establish his or her own conclusions about the validity. For example, admission data, other social history along with any significant medications taken, the clinical manifestations after the first TACE, images about the first TACE after remasking and pixel shifting.

#4. All the references cited should be critically evaluated. Review articles should not be used as good references. For example, citations for 11 and so on.

#5. There are few references in recent years.

#### Response to reviewer 02439215

Thank you very much for your review of our manuscript.

According to the comments #1 and #3, we have made corrections and additions to our manuscript in the CASE REPORT section, but we cannot obtain the images about the first TACE.

A 63-year-old man with a large recurrent HCC replacing most of the lateral segment of the liver and expanding to the left diaphragm was admitted to our hospital for a second TACE. He had a history of type-B cirrhosis for 3 years. Eight months prior to admission, he had undergone TACE for the same lesion via the left hepatic artery (LHA), and the postprocedural course was uneventful. Laboratory tests before second TACE revealed a serum total bilirubin level of 1.4 mg/dl, serum albumin level of 3.0 mg/dl, and prothrombin activity level of 81%. Neither ascites nor hepatic encephalopathy were found, which corresponded to Child-Pugh class A. The  $\alpha$ -fetoprotein level was 900 ng/mL.

**According to the comment #2,** we have made corrections and additions to our manuscript in the Introduction section.

This is the first report of CLE, in which the vascular lake phenomenon emerged during the TACE procedure and caused an intratumoral arteriovenous shunt, playing the most important role in its occurrence.

**According to the comments #4 and #5,**

We updated the list of cited references. The table has also been updated accordingly, and detailed numerical values in the text have also been updated.