

Dear Editor

Please find enclosed our response to the reviewers' comments. The manuscript has been modified accordingly and reedited by a native speaker professional editor. We would like to thank the reviewers for their comments that helped us to improve the quality of the manuscript.

We thank you once again for considering our article for publication in your journal.

Reviewer # 1 (Comments to the Author):

This article title with 'Esophageal metastasis of stem-cell subtype hepatocholangiocarcinoma: atypical presentation of a rare tumor' it should be published at WJG. It has new informations and it makes a new contribution for understanding of hepatocellular carcinoma.

We thank you for these comments.

Reviewer #2 (Comments to the Author):

1. The authors should elaborate more why this tumor was classified as stem-cell subtype and whether this subtype has different prognosis and therapeutic outcome. What type of stem cell this tumor originates?

This tumor was classified as stem-cell subtype according to the WHO classification, with the presence of pathological details as described in Table 1. The presence of small cells leads to the diagnosis of stem cell subtype (comment added page 6). The prognosis according to different subtypes is unknown.

The origin of these stem cells is still discussed, with some studies suggesting an origin from hepatic progenitor stem cells with a double dedifferentiation potential in hepatocytes and cholangiocytes.

2. The authors state: "biopsies should be advocated in case of biological or imaging features suggesting an hepatocholangiocarcinoma". Why? Is there a different treatment?

It is important to obtain a correct diagnosis. The managements of cholangiocarcinoma and hepatocellular carcinoma are different. There are few data about the management of hepatocholangiocarcinoma, some studies suggest a poor prognosis after liver transplantation and a chemosensitivity to gemcitabine + platinum. A comment has been added page 8.

3. Figures 2 and 3 should be clearly marked e.g. with arrows or asterisks – this would enhance their didactic value.

The marks have been added.

4. The paper requires a careful linguistic and stylistic revisions. e.g. “one wasting week of rest before new cycle” delete wasting “showed a 10-cm polypoid tumor, located in the lower third of the esophagus, about 30 cm from the upper dental arch. “ should be 10 cm long from incisors

The manuscript has been reedited by a english native speaker professional editor (Kate Vassaux).

5. The authors may consider adding references listed below Serra V, et al. Incidental Intra-Hepatic Cholangiocarcinoma and Hepatocholangiocarcinoma in Liver Transplantation: A Single-Center Experience. Transplant Proc. 2016 Mar;48(2):366-9. doi: 10.1016/j.transproceed.2015.12.044. PMID: 27109957 Potretzke TA et al. Imaging Features of Biphenotypic Primary Liver Carcinoma (Hepatocholangiocarcinoma) and the Potential to Mimic Hepatocellular Carcinoma: LI-RADS Analysis of CT and MRI Features in 61 Cases. AJR Am J Roentgenol. 2016 Jul;207(1):25-31. doi: 10.2214/AJR.15.14997. Epub 2016 Feb 11. PMID: 26866746

These references have been added page 7 and 8.

Reviewer #3 (Comments to the Author):

The authors present a rare case of hepatocholangiocarcinoma with esophageal metastasis. Indeed, the diagnosis of this primary liver tumor is difficult even combination of imaging, biomarker and histology, not mention with esophageal

metastasis. One minor concern is that the description of WHO 2010 classification is not easy to understand in accordance to histology of present case, especially for whom is not a pathologist.

The reviewer is right, this WHO classification is complex but is poorly known, and we believe that it is worth being mentioned in the manuscript.