

Dear editor:

We would like to thank World Journal of Gastroenterology for giving us the opportunity to revise our manuscript.

We thank the reviewers for careful read and thoughtful comments on previous draft. We have carefully taken their comments into consideration in preparing our revision, which has resulted in a paper that is clearer, more compelling, and broader. Revised portion are marked in blue and the deleted parts are added with a strikethrough in the paper. The following summarizes how we responded to reviewer comment.

Below is our response to their comments.

Thanks for all the help.

Best wishes,

Zhi-Qun Mao

Reviewer #1:

STATUS: ACCETTABLE FOR PUBBLICATION PENDING MINOR REVISIONS

Short summary according reviewer: Authors reported two cases of inflammatory pseudotumor-like follicular dendritic cell (IPT-like FDC) tumor of the liver, an uncommon tumor with extremely low incidence. Imaging findings, especially CT and MRI features, were described. General considerations + Study design: This is a CASE REPORT article. The paper is well-written. The work is very interesting and there are only a few articles in literature about this topic. Abstract: the abstract appropriately summarize the manuscript without discrepancies between the abstract and the remainder of the manuscript. Key points: adequate. Keywords: adequate.

Paper On some aspects, the authors should address:

1). In my opinion, you focused too much on CT and MR findings. Why don't you also deal the role of ultrasound? I understand that your article focuses on the role of CT and MRI in the diagnosis of these lesions, but I think it is more appropriate to point out that focal liver lesion are discovered firstly on US examination, which in many countries is the first choice in the study of the liver and, more generally, of the abdomen. You can refer to the following articles, which you have to discuss and cite:

-Harvey CJ, Albrecht T. *Ultrasound of focal liver lesions. Eur Radiol. 2001;11(9):1578-93.*

-Corvino A, Sandomenico F, Setola SV, Corvino F, Tafuri D, Catalano O. *Morphological and dynamic evaluation of complex cystic focal liver lesions by contrast-enhanced ultrasound: current state of the art. J Ultrasound. 2019 Sep;22(3):251-259. doi: 10.1007/s40477-019-00385-2. Epub 2019 May 13.*

-Corvino A, Catalano O, Corvino F, Petrillo A. *Rectal melanoma presenting as a solitary complex cystic liver lesion: role of contrast-specific low-MI real-time ultrasound imaging. J Ultrasound 2015;19(2):135-9. doi: 10.1007/s40477-015-0182-*

1. eCollection 2016.

Response: Thanks for thoughtful suggestions and references. we agree that ultrasound is important and often the first test to evaluate liver tumor. In the revised version, we moved the discussion about US to the front of the discussion of CT and MRI. Moreover, we have carefully read the above references and cited relevant knowledge (Please see Page 12, Line 309 to Line 313). In addition, we also simplified the characterization of CT and MRI (Please see Page 12, Line 314-319; Page 13, Line 327-331 and Line 339-341) and made a table to summarize the relevant image features (Please see Page 21, Line 424).

2). Similarly, you have described in detail CT and MR imaging findings. Why didn't you also consider to discuss about CEUS? Have you got any experience? I advise you not to neglect this aspect, which in my opinion is fundamental. Considering the results obtained by CEUS, I believe that a reference is needed in the discussion. Consider the following articles about, which you must cite:

-Corvino A, Catalano O, Corvino F, Sandomenico F, Petrillo A. Diagnostic Performance and Confidence of Contrast-Enhanced Ultrasound in the Differential Diagnosis of Cystic and Cysticlike Liver Lesions. *AJR Am J Roentgenol* 2017;209(3):W119-W127. doi: 10.2214/AJR.16.17062. Epub 2017 Jun 22.

-Corvino A, Catalano O, Setola SV, Sandomenico F, Corvino F, Petrillo A. Contrast-enhanced ultrasound in the characterization of complex cystic focal liver lesions. *Ultrasound Med Biol* 2015;41(5):1301-10. doi: 10.1016/j.ultrasmedbio.2014.12.667. Epub 2015 Feb 7.

Response: We appreciate the reviewer's suggestion on discussing about CEUS. Unfortunately, CEUS was not performed in these 2 cases. In our country, the Department of Ultrasound and Radiology are two different departments. So far, we do not have experience on CEUS. Hopefully with cooperation of our ultrasound

department, we are able to use CEUS to assess liver tumors in the future. Moreover, we added the relevant content in the paragraph of differential diagnosis ([Please see Page 13-14, Line 346 - 356](#)). We appreciate your understanding.

3). What are the technical parameters used in the the study? I think it would be necessary at least to mention some acquisition protocols currently used in computed tomography and magnetic resonance. You can find a routinary multidetector row multi-slice CT and magnetic resonance acquisition protocol in the following articles, which you must cite in the reference:

-Corvino A, Corvino F, Radice L, Catalano O. Synchronous mucinous colonic adenocarcinoma and multiple small intestinal adenocarcinomas: report of a case and review of literature. Clin Imaging. 2015 May-Jun;39(3):538-42. doi: 10.1016/j.clinimag.2014.12.019. Epub 2015 Jan 7.

-Maurea S, Corvino A, Imbriaco M, Avitabile G, Mainenti P, Camera L, Galizia G, Salvatore M. Simultaneous non-functioning neuroendocrine carcinoma of the pancreas and extra-hepatic cholangiocarcinoma. A case of early diagnosis and favorable post-surgical outcome. JOP 2011;12(3):255-8.

Response: Thanks for your suggestion and references. We have added some parameters using in CT and MRI based on the information in references. ([Please see Page 7-8, Line 180-189 ; Page 10, Line 246-253](#))

4). Why don't you discuss about the pseudolesions, which can occur. In this regard, I invite you to read the following articles citing them:

-Elsayes KM, Menias CO, Morshid AI, Shaaban AM, Fowler KJ, Tang A, Chernyak V, Szklaruk J, Bashir MR. Spectrum of Pitfalls, Pseudolesions, and

Misdiagnoses in Noncirrhotic Liver. AJR Am J Roentgenol. 2018 Jul;211(1):97-108. doi: 10.2214/AJR.18.19820.

-Guarino B, Catalano O, Corvino A, Corvino F, Amore A, Petrillo A. Hepatic inflammatory pseudotumor: educational value of an incorrect diagnosis at contrast-enhanced ultrasound. J Med Ultrason 2015;42(4):547-52. doi: 10.1007/s10396-015-0624-6. Epub 2015 Mar 27.

Response: Thanks for your suggestion and references. It is thoughtful to have broad differential diagnosis including pseudolesions. We have read the above references and added some relevant content about IPT. [*\(Please see Page 13, Line 347 - 350\).*](#)

5). In the Introduction paragraph you wrote: “The inflammatory pseudotumor-like follicular dendritic cell(IPT-like FDC) tumor is a variant subset of follicular dendritic cell (FDC) tumor. The FDC tumors most commonly occur in the cervical lymph nodes, which are extremely rare in the liver and representing <0.1 % of all primary hepatic tumors”. In the Discussion paragraph you wrote: “The IPT-like FDC tumor is an extremely rare and low-grade malignant soft tissue sarcoma that occurs almost exclusively in the liver and spleen”. There would seem to be a discrepancy. Please, specify it.

Response: Thank you for your careful reading of our manuscript. We sincerely apologize for the misunderstanding caused by our lack of clarity. In order to make the statement more concise, we deleted the sentence “that occurs almost exclusively in the liver and spleen” in the discussion. [*\(Please see Page 11, Line 279\).*](#)

6). HCC and metastases are the main differential diagnoses. Do you have any examples which resembling IPT-like FDC? Please, discuss it in the text. Consider the following articles about:

-Corvino A, Catalano O, Corvino F, Petrillo A. Rectal melanoma presenting as a solitary complex cystic liver lesion: role of contrast-specific low-MI real-time ultrasound imaging. J Ultrasound 2015;19(2):135-9. doi: 10.1007/s40477-015-0182-

1. eCollection 2016.

-Guarino B, Catalano O, Corvino A, Corvino F, Amore A, Petrillo A. Hepatic inflammatory pseudotumor: educational value of an incorrect diagnosis at contrast-enhanced ultrasound. *J Med Ultrason* 2015;42(4):547-52. doi: 10.1007/s10396-015-0624-6. Epub 2015 Mar 27.

-Corvino A, Sandomenico F, Setola SV, Corvino F, Tafuri D, Catalano O. Morphological and dynamic evaluation of complex cystic focal liver lesions by contrast-enhanced ultrasound: current state of the art. *J Ultrasound*. 2019 Sep;22(3):251-259. doi: 10.1007/s40477-019-00385-2. Epub 2019 May 13.

Response: Thanks for your suggestion and references. We have read the above references and cited some relevant content about HCC and metastases in discussion. [\(Please see Page 13-14, Line 350-356\).](#)

7). Reference: the references are adequate.

8). Tables: Why don't you create a table of CT and MR findings?

Response: Thanks for your advice. We have added a table of CT and MRI findings. [\(Please see Page 21, Line 424\).](#)

9). Figures: 1) images are good. 2) If you have, why don't you insert some images of CEUS of same cases?

Response: Thanks for your comment. As mentioned comment #2, these two patients did not perform CEUS.

10). Figure 1. -In Figure 1 you used the terms rapid wash in (it may be correct) and slow wash-out but I see wash-out already in the portal phase (B). Why do you talk about slow wash-out? Please specify the acquisition times and study phases. - In Figure 1, in the most anterior lesion I do not see internal necrosis. I am wrong?

Response: Thanks for your good question. We sincerely apologize for the confusion caused by our mistake. In order to better understand the “wash out”, we consulted some

relevant literature^[1, 2, 3]. Washout was defined as less contrast enhancement of the tumor on portal, hepatic venous, and equilibrium phase images than on arterial phase images^[1, 2]. Sustained enhancement occurred if the lesion showed enhancement in the arterial phase and greater or equal enhancement in the portal venous phase relative to that of the liver^[1, 3]. We found that there is a bias in our understanding. So the statement of “heterogeneous marked enhancement with ‘rapid wash in and slow wash out’ patterns,” was corrected as “heterogeneous sustained hypoenhancement”. *(Please see Page 4, Line 97-98, Line 108-109 and Line 114-115; Page 12, Line 314-316; Page 14, Line 367-368; Page 15, Line 376-377; Page 17, Line 395-396; Page 20, Line 418-419).*

We confirmed the scan parameters and added them into the article. *(Please see Page 7-8, Line 180-189; Page 10, Line 246-253)*

In addition, the necrosis in the smaller tumor of case 1 was indeed not well recognized. But when we enlarged the figure 1, we could see scattered spots hypodensity, and the pathology also confirmed the existence of necrosis inside the tumor.

1. Burns, P. N. and S. R. Wilson (2007). "Focal liver masses: enhancement patterns on contrast-enhanced images--concordance of US scans with CT scans and MR images." *Radiology* 242(1): 162-174.

2. Jeong, H. T., et al. (2013). "Gadoxetate disodium-enhanced MRI of mass-forming intrahepatic cholangiocarcinomas: imaging-histologic correlation." *AJR Am J Roentgenol* 201(4): W603-611.

3. Kim, R., et al. (2015). "Differentiation of intrahepatic mass-forming cholangiocarcinoma from hepatocellular carcinoma on gadoxetic acid-enhanced liver MR imaging." *European Radiology* 26(6): 1808-1817.

11). Figure 2. -In Figure 2 you used the terms rapid wash in (it may be correct) and slow

wash-out, but I see wash-out already in the portal phase (B). Why do you talk about slow wash-out? Please specify the acquisition times and study phases.

Response: Thanks for your good question. This question is similar to the previous one, we have already explained it. Please refer to the above response. Apologize again for the confusion we caused.

12). Figure 3. Why is US presented at the end?

Response: Thanks for your comment. We have placed the content of the ultrasound in the first position in the section of **Imaging examinations** (*Please see Page 7, Line 177-179*) and then reordered the images according to the order in which they appear. (*Please see Page 16, Line 382*).

Figure 5. I still don't understand why you talk about slow wash-out. In the portal phase the lesion is hypodense.

Response: Thanks for your comment. This question is similar to the comment 10 and 11, please refer to the above response. Apologize again for the confusion we caused.

14). Figure 6. Why is US presented at the end?

Response: Thanks for your comment. We have placed the content of the ultrasound in the first position in the section of **Imaging examinations** (*Please see Page 10, Line 243-245*) and then reordered the images according to the order in which they appear. (*Please see Page 19, Line 409*).