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Reviewer's code: 03656596

SPECIFIC COMMENTS TO AUTHORS

From the information provided by the case, it is very easy to be confused clinically. The publication of this article is meaningful.

RESPONSE TO REVIEWER

Thank you very much for your comment. We appreciate your consideration for suitability for publications in World Journal of Gastroenterology

Reviewer's code: 03317331

SPECIFIC COMMENTS TO AUTHORS

This is an interesting case report about the cystic liver metastasis of renal cell carcinoma. I have some comments: 1. Because ths patient has bilateral lobes of liver cysts in 4 years ago (before operation for left renal cell carcinoma), the image of previous abdominal CT should be presented. Then we could compare the change of liver cystic lesions between 4 years ago (before resection of left left renal cell carcinoma) and current status (before hepatectomy for "cystic" metastatic renal cell carcinoma). 2. If liver cysts (or cystic tumors) have been existed for 4 years, it is possible that renal cell carcinoma has been "cystic" metastatis to liver in 4 years ago. Or it is just a condition that renal cell carcinoma develops metastasis in a liver with polycytic liver disease (PCLD). The author should elucidate these conditions because there was no "cystic" liver metastasis reported in PRCC patients. 3. This patient received an operation (liver right lobectomy) for recurrent hemorrage of liver cysts. The author though this operation might be avoid if the diagnosis of metastatic RCC could be made before operation. But how to get a correct pre-operation diagnosis for a patient with polycystic liver disease? Repeated fine needle aspiration for cytology study

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or core biopsy for pathologic examination? And how to treat the symptom of abdominal pain for this patient if liver cytic metastasis diagnosed before operation? The author should be further explained in the discussion section. 4. Could the author further report the prognosis of this patient after operations for right lobe hepatectomy and cyst fenestration? According to the current report, the patient started sunitinib treatment 1 month after the hepatectomy. If the pain was relived and the life quality was improved for this patient?

RESPONSE TO REVIEWER

Thank you very much for your excellent comments. We got English corrections from the company WJG is recommending. Certification for English correction is attached. We changed the contents following your comments.

1. Because this patient has bilateral lobes of liver cysts in 4 years ago (before operation for left renal cell carcinoma), the image of previous abdominal CT should be presented. Then we could compare the change of liver cystic lesions between 4 years ago (before resection of left left renal cell carcinoma) and current status (before hepatectomy for "cystic" metastatic renal cell carcinoma).

=> We presented the CT image 4 years prior to surgery (Figure 1A). "There was one large cyst and several small cysts, as demonstrated by a CT scan. The liver cysts appeared as well-demarcated and water-dense sacs without mural nodules." We added these descriptions at Case presentation section. Compared with the CT images 4 years ago, the number and size of cysts had increased, but there was no change in characteristics in cystic walls, implying of malignancy.

2. If liver cysts (or cystic tumors) have been existed for 4 years, it is possible that renal cell

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carcinoma has been "cystic" metastatis to liver in 4 years ago. Or it is just a condition that renal cell carcinoma develops metastasis in a liver with polycytic liver disease (PCLD). The author should elucidate these conditions because there was no "cystic" liver metastasis reported in PRCC patients.

=> Since immunohistochemical staining for all the liver cysts showed presence of CD 10 and no presence of CK7$^+$ and CK19$^+$ cells in the edges of the cysts in pathological report, we think the PRCC had metastasized to the liver already 4 years prior to the surgery. However, because there was no sign of malignancy, i.e., no hypertrophy, irregularity or mural nodule of cyst walls, it was difficult to distinguish it from PCLD at that time (Figure 1A). We don't think cystic metastasis happened to PCLD liver since all the cysts pathologically investigated showed malignant characteristics. We added "It was quite unlikely that cystic liver metastasis occurred to a liver affected by PCLD, since all the cysts that were pathologically investigated showed the malignant characteristics described above." at the discussion section.

3. This patient received an operation (liver right lobectomy) for recurrent hemorrhage of liver cysts. The author though this operation might be avoid if the diagnosis of metastatic RCC could be made before operation. But how to get a correct pre-operation diagnosis for a patient with polycystic liver disease? Repeated fine needle aspiration for cytology study or core biopsy for pathologic examination? And how to treat the symptom of abdominal pain for this patient if liver cystic metastasis diagnosed before operation? The author should be further explained in the discussion section.

=> According to the literature, it was reported that CA 50 could be a potential marker for detecting cystic PRCC [1]. Further, 18F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) was shown to detect cystic liver metastasis of a nasopharyngeal cancer [2]. Thus, we could have tested the CA 50 in the blood and the

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cystic fluid by repeated fine needle aspiration. Also, we could have checked PET/CT scan to confirm the malignancy of the cysts if we had taken metastasis into consideration. We added these descriptions in discussion section.

Regarding treatment for this patient, we should have started with chemotherapy with palliative care, using opioids and additional adjuvants to alleviate the abdominal symptoms. This is because complete resection is the only choice for patients with metastatic RCC, and in cases with bilateral multiple metastatic RCC, such as our case, are not candidates for hepatectomy because radical resection cannot be performed, and the surgery will not prolong the overall survival time of the patients. We added all these descriptions at the Discussion section.

[1] Ljungberg B, Holmberg G, Sjodin JG, Hietala SO, Stenling R. Renal cell carcinoma in a renal cyst: a case report and review of the literature. The Journal of urology 1990; 143(4): 797-799 [PMID: 2179585]

[2] Radhakrishnan V, Thulkar S, Karunanithi S, Tanveer N, Bakhshi S. Nasopharyngeal carcinoma with splenic and cystic liver metastases in a pediatric patient: 18F-FDG PET-CT findings. Pediatr Radiol 2010; 40 Suppl 1: S79-82 [PMID: 20922367 DOI: 10.1007/s00247-010-1844-y]

4. Could the author further report the prognosis of this patient after operations for right lobe hepatectomy and cyst fenestration? According to the current report, the patient started sunitinib treatment 1 month after the hepatectomy. If the pain was relived and the life quality was improved for this patient?

=> "It has been 2 years since the surgery was performed. The pain was relived after the surgery, and the patient is still alive. However, lymph node metastases and lung metastases appeared after a few months, and the cysts occupying the remnant liver are growing, causing recurrent abdominal pain. The patient is now managed with

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symptomatic treatment." We added this description at the end of Case presentation section.