

Round 1

Reviewer #2:

1. First, the private information of the patient was found in Fig. 1. It should be deleted immediately.

Response: Thanks a lot! We have modified the figure as this comment suggested.

2. The standard chemotherapy for ICC is GEM+CDDP. Authors should describe or discuss the reason why GEM+S1 is selected in present case.

Response: Thanks a lot! Because of the lower side effect and higher tolerance, we chose Gemcitabine + capecitabine more often in our hospital. The patient experienced III hand-foot syndrome. Then capecitabine was replaced by S1.

3. The pathway of metastasis to brain should be discussed. In present case, no LN metastases were found. Authors should show and discuss the histopathological findings of primary lesion more detail.

Response: This observation highlights the complex and heterogeneous nature of the disease. Due to the rare occurrence of the brain metastasis from ICC, an international sample bank, which needs worldwide cooperation of the involved institutions, will contribute to untangling the complex pathogenesis using omics- and system-based methodologies, and therefore to clarify the underlying mechanism behind this.

4. Authors should describe neurological findings of the patient after surgical resection.

Response: Thanks a lot! We have added the findings as this comment suggested.

Reviewer #3:

Abstract section: 1)line 30:"than 40 cases have been described in the literature to date" this phrase should be moved in the introduction section,

Response: Thanks a lot! We have modified the text as this comment suggested.

2)line 32:""Tumor markers were normal. Serological analysis indicated absence of hepatitis virus." this phrase should be moved after" Abdominal computed tomography showed a lesion in the left lobe of the liver. furthermore indicate the size and the segment of the nodule.

Response: Thanks a lot! We have modified the text as this comment suggested.

3)line 37:the size of the brain nodule should be reported.

Response: Thanks a lot! We have modified the text as this comment suggested.

4)line 37:I do not understand this statement! In the abstract shuol be reported as diagnosis was obtained!!!

Response: Thanks a lot! We have modified the text as this comment suggested.

CASE presentation section

1)line 70a"abdominal compted tomography": please add " with contrst media and describe the vascula findings of the liver lesion,the size and the segment location:tha vascular findings should be reported also in the legend of figures regardind the CT examination.The same is due for the vascular characteristic

of the brain lesion.

Response: Thanks a lot! We have modified the text as this comment suggested.

2) indicate the type of biopsy of the liver lesion:cutting needle and what gauge.

Response: Thanks a lot! We have modified the text as this comment suggested.

3)line 76:again !authors should describe the result of the liver biopsy ,report the type of ICC (if obtained with biopsy and, anyway indicated after the surgical operation) and hypothesize the presence of the brain nodule as a possible metastasis of the ICC.

Response: Thanks a lot! We have modified the text as this comment suggested. The brain lesion had hyperintensity in T1 image and hypointensity in T2 image. There was obvious edema zone around the lesion. Those results showed that the lesion had the feature of metastasis.

reference section references should be changed according to the standard of the Journal

Response: Thanks a lot! We have modified the references as this comment suggested.

Round 2

1. Post operation period should be clarified (33 or 39 months).

Response: Thanks a lot! We have checked the post operation period. During a 39-months postoperative follow-up, no sign of local recurrence or distant metastasis was observed.

2. The reason of decision by MDT should be shown (the indication of operation, the selection and the timing of chemotherapy).

Response: Thanks a lot! Surgery-based comprehensive treatment was recommended by our liver cancer MDT for the following reasons. First, there was an opportunity for complete resection of both the primary and metastasis lesions, and no lymph node metastasis was found, which is strongly associated with surgical prognosis [10]. Second, brain radiotherapy may exacerbate compression symptoms and the primary liver lesion may progress during therapy. Third, chemotherapeutic drugs may not cross the blood-brain barrier; additionally, there are reports that resection of brain metastatic lesions from ICC did improve survival time. Four weeks after surgery, the combination chemotherapy was given because the patient had distant metastasis.