



PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 34331

Title: Case of primary biliary cholangitis metachronously complicated with combined hepatocellular carcinoma-cholangiocellular carcinoma and hepatocellular carcinoma

Reviewer's code: 02936296

Reviewer's country: United States

Science editor: Jin-Xin Kong

Date sent for review: 2017-06-19

Date reviewed: 2017-06-21

Review time: 1 Day

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> [Y] Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> [Y] Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> [] High priority for publication
<input type="checkbox"/> [Y] Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> [] Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> [] Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> [Y] No	<input type="checkbox"/> [] Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> [Y] No	

COMMENTS TO AUTHORS

Primary biliary cirrhosis (PBC) is a chronic and progressive cholestatic disease of the liver. Some cases of PBC complicated by HCC have been previously reported. In this report, the authors present a case of PBC metachronously complicated by cHCC-CCC and HCC. The authors concludes that in patients with PBC, it is necessary to check up not only liver function but also carcinogenesis including HCC, CCC and cHCC-CCC. 1. This case report is well organized and clearly describes the clinical information. But the discussion section needs to be strengthened. Disease diagnosis, differential diagnosis, treatment, and experiences need to be thoroughly discussed. 2. The multi-centric tumorigenesis resulted from PBC is rarely reported and would be of interest to the specialists in the field. It is advisable to further perform biomolecular studies based on different tumor specimens.



PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 34331

Title: Case of primary biliary cholangitis metachronously complicated with combined hepatocellular carcinoma-cholangiocellular carcinoma and hepatocellular carcinoma

Reviewer's code: 03473431

Reviewer's country: Italy

Science editor: Jin-Xin Kong

Date sent for review: 2017-06-19

Date reviewed: 2017-06-24

Review time: 5 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

the authors present a very rare and interesting case of combination of HCC and ICC in cirrhosis and a metacronous case of HCC. The appearance of cHCC-ICC in cirrhosis is rare even in large cohorts and generally it appears in viral (HBV and/or HCV) infected patients. Some changes should be made. 1) First of all ,the term primary biliary cirrhosis should be changed in the recent EASL/AASLD proposed term "PRIMARY BILIARY COLANGITIS". 2) was Ca125 detected in both the cases? 3) was CEUS performed in the patient? if not explain.If yes report the CEUS findings? Did authors use Sonovue or Sonoazoid? 4)Authors should better explain why they chose surgery in their patient.Their explanation appears too simplistic: the first nodule was clearly visible on US and, considering the specific patterns of enhanced CT and MRI for HCC in cirrhosis, percutaneous RF ablation in a 74 years old patient should be the best approach.On



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the other hand, was percutaneous US guided biopsy considered prior to surgery? the same thing for the second nodule. 5) the 2 tables with laboratory data are unnecessary. 6) figures are good 7) references should be updated: consider and discuss in the discussion section: Incidental Intra-Hepatic Cholangiocarcinoma and Hepatocholangiocarcinoma in Liver Transplantation: A Single-Center Experience. Serra V, Tarantino G, Guidetti C, Aldrovandi S, Cuoghi M, Olivieri T, Assirati G, De Ruvo N, Magistri P, Ballarin R, Di Benedetto F. *Transplant Proc.* 2016 Mar;48(2):366-9. doi: 10.1016/j.transproceed.2015.12.044. and Combined hepatocellular carcinoma and cholangiocarcinoma (biphenotypic) tumors: clinical characteristics, imaging features of contrast-enhanced ultrasound and computed tomography. Li R, Yang D, Tang CL, Cai P, Ma KS, Ding SY, Zhang XH, Guo DY, Yan XC. *BMC Cancer.* 2016 Feb 25;16:158. doi: 10.1186/s12885-016-2156-x.



PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 34331

Title: Case of primary biliary cholangitis metachronously complicated with combined hepatocellular carcinoma-cholangiocellular carcinoma and hepatocellular carcinoma

Reviewer's code: 00069837

Reviewer's country: Argentina

Science editor: Jin-Xin Kong

Date sent for review: 2017-06-19

Date reviewed: 2017-07-02

Review time: 12 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

This is an original and interesting paper describing a liver tumor on liver cirrhosis that has never been previously reported. However, several changes and corrections should be carried out before publication 1- The name Primary biliary cirrhosis should be replaced by Primary biliary cholangitis in title and text since in the new nomenclature the word "cirrhosis" was changed to "cholangitis" (Beuers U. et al. Changing Nomenclature for PBC: From 'Cirrhosis' to 'Cholangitis. Am J Gastroenterol 2015; 110:1536-1538) 2- Dynamic characteristics and contrast behavior of cHCC-CCC in the arterial and venous phase of TC and RMI should be more deeply described by authors within the "Case report section". A better description at this point could help the reader to understand more why a resection of small tumor associated with normal serum level of tumor markers was carried out 3- A potential metabolic syndrome as a risk factor



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for carcinogenesis was raised by authors within "discussion section". However, a diagnosis of metabolic syndrome in absence of both serum insulin level and HOMA score determination in patients with normal BMI is very difficult to understand. This paragraph should be modified or removed from the text 4- Where authors say in the discussion section "In the present case, as Theise et al. indicated, the result of EpCAM immunohistochemistry (a stem cell marker), might be consistent with that of mixed type cHCC-CCC", a bibliographic reference is lacking. 5- Normal range of liver function tests are lacking within table 1 6- Data are not clearly showed in Table 1. Two tables with separate data should be carried out



PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 34331

Title: Case of primary biliary cholangitis metachronously complicated with combined hepatocellular carcinoma-cholangiocellular carcinoma and hepatocellular carcinoma

Reviewer's code: 02908399

Reviewer's country: Pakistan

Science editor: Jin-Xin Kong

Date sent for review: 2017-06-19

Date reviewed: 2017-07-02

Review time: 12 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The authors have reported a single case of a PBC female patient with development of liver related tumors over a 24 year period. Please clarify the following. 1) Was this patient under surveillance or screening since the first liver mass she developed was found incidentally? Are there any screening recommendations in PBC patients? 2) The first tumor was resected along with part of MHV. Was the vein involved on histopathology? If it was, was a partial resection considered appropriate treatment? 3) Later, partial resection of another liver segment was performed. Do you think this patient would benefit from more radical procedures like liver transplant for example. I understand that she is not cirrhotic and has no decompensations but she has had multiple tumors with one possibly involving MHV. 4) What is her follow up routine post resection? 5) Was any adjuvant chemo given to her? Thank you