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Wan Chai, Hong Kong, China

ESPS Peer-review Report
Name of Journal: World Journal of Gastrointestinal Surgery
ESPS Manuscript NO: 7649
Title: Pancreatic and Pulmonary Recurrences of Intrahepatic Cholangiocarcinoma after Liver Resection: A Case Report and a Review of the Literature
Reviewer code: 00005858
Science editor: Wen, Ling-Ling
Date sent for review: 2013-11-28 10:15
Date reviewed: 2013-11-29 15:51

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[Y] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
It is an interesting case report and well documented. However, there are some issues that need to be address. 1) Concerning the diagnosis of intrahepatic cholangiocellular carcinoma (ICC). Based on the pathological picture, cholangiolocellular carcinoma (CLC) can be a differential diagnosis. CLC can happen in hepatitis virus positive patients and its location is mainly seen in the periphery of the liver (ref. 1). Absent intrahepatic bile duct dilatation is also fit with CLC as it arises from the smallest bile duct/ductules/hepatic progenitor cells. It is very important to distinguish between CLC and ordinaly ICC (mucin producing ICC) as they show completely different clinicopathological-radiological-genetical features (ref. 2). Please clarify this point. References 1) Hepatology. 2008 May;47(5):1544-56. 2) Hepatology. 2012 Jun;55(6):1876-88. 2) We can't exclude completely the possibility that the cancer located in the pancreatic tail can be directly invaded by adjacent lymph node metastasis. Because the distinction can be challenging by imaging. In addition, as the authors mentioned in the article; the dissemination pattern remains unclear in this case. Please clarify this point. 3) It would be better to mention the pathological picture of metastatic lung tumor to show that it is metastatic from ICC.

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ESPS Manuscript NO: 7649
Title: Pancreatic and Pulmonary Recurrences of Intrahepatic Cholangiocarcinoma after Liver Resection: A Case Report and a Review of the Literature
Reviewer code: 02461732
Science editor: Wen, Ling-Ling
Date sent for review: 2013-11-28 10:15
Date reviewed: 2013-12-03 05:46

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
Dr. Labgaa et al. describe a case of intrahepatic cholangiocarcinoma in a young patient with a history of HBV. The lesion was initially suspected to be HCC. Analysis after resection revealed an adenocarcinoma consistent with cholangiocarcinoma. Four years after resection, a pancreatic lesion and multiple lung nodules were discovered, and were treated with systemic chemotherapy. The patient had a response to treatment, and is currently still alive. This is an interesting case and the manuscript is well written. There are a number of unexpected or unusual aspects to this case. First, the patients age and (as the authors note) lack of a classical risk factor for ICC. HBV seems to be this patients risk factor. Next, the metastatic site of the pancreas is unexpected for a tumor that was considered node-negative and intrahepatic. Additionally, there is an uncertain association to her pregnancy. Finally, the good response to systemic chemotherapy is fortunate, if not expected. I would ask for some additional information, and a revision of the discussion, as outlined below: 1. I would like a bit more information about the patient. Specifically, the manuscript indicates the patient is Chinese. Is she living in the US or did she travel for treatment? If she is living in the US, is she a recent immigrant, long-time immigrant, or US-born of Chinese descent? Was she tested for ova and parasites (e.g. liver fluke infestation)? Based on the report, she is G2P1A0, however it is not clear that her full pregnancy history is given; to fully judge any association, please include her pregnancy history explicitly. 2. Were any special stains done of the primary tumor and also on the metastatic tissues? Did these match? Was HBV staining of the mets done? 3. Was AFP or CA19-9 tested in the serum? AFP staining of the primary and metastatic tumors? Serum markers upon recurrence? 4. The discussion should consider additional possible explanations for the findings. Because the

pancreas is an unusual site for metastasis, it is possible the liver tumor was not primary, but possibly itself was a metastatic lesion from an unknown primary. Thus the diagnosis of cholangiocarcinoma is likely, but not certain. In a young female patient, metastatic breast cancer could be considered. 5. Alternatively, the newly diagnosed (pancreatic and lung) tumors may represent a second primary tumor that is metastatic on diagnosis. It is not clear how a second primary malignancy was considered versus metastasis of the original ICC (special stains?). This should be included in the discussion. 6. Finally, Fig 2A has a hand-written specimen number and date. These should probably be removed (easily cropped out of the image without losing the ruler marks), in case they uniquely identify the patient and compromise privacy.

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Name of Journal: World Journal of Gastrointestinal Surgery
ESPS Manuscript NO: 7649
Title: Pancreatic and Pulmonary Recurrences of Intrahepatic Cholangiocarcinoma after Liver Resection: A Case Report and a Review of the Literature
Reviewer code: 02649114
Science editor: Wen, Ling-Ling
Date sent for review: 2013-11-28 10:15
Date reviewed: 2013-12-16 10:12

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[Y]Rejection
[Y] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

The authors report a case of cholangiocarcinoma that metastasized to the pancreas and lungs. This occurred in a young woman with chronic hepatitis B. The metastases were detected almost 4 years after her cholangiocarcinoma was resected. While this is an interesting case, the diagnosis of pancreatic metastasis can only be speculative. At the maximum, we can only say that the pancreatic cancer likely represents metastatic cholangiocarcinoma. However, the possibility of a new pancreatic primary cannot be completely ruled out (although it is also rare to have pancreatic ductal adenocarcinoma at the young age). It is difficult to make a morphologic comparison between histologic section for original cholangiocarcinoma (Fig. 2B) and FNA cytology for pancreatic tumor (Fig. 3) to ascertain that they are the same tumors. Although there are no reliable biomarkers that distinguish primary pancreatic adenocarcinoma from metastatic cholangiocarcinoma, efforts should be made to determine whether the tumors in the liver and the pancreas in this young patient are immunohistochemically or molecularly similar or distinctive. Markers such as KRAS, HER2 and SMAD4 may be useful in this regard. It is true that metastatic cholangiocarcinoma to the pancreas is a rare occurrence. It has been documented in at least one previous publication (Yoon WJ, et al. Gut Liver. 2011; 5:61-4). This is thus not “never been reported” or “the first” as authors claimed.