

Reviewer's code: 00068153

Neuroendocrine neoplasm in the liver is not a common disease. According to the authors, this is the largest study so far describing detailed histological findings and relevant clinical data of patients with hepatic neuroendocrine neoplasms. The authors had drawn some valuable conclusions for this disease

Reply: Thank you.

Reviewer's code: 01550488

The authors report here on the pathological data of 79 patients with liver-metastasis of NET (including maybe a few primary liver NET's, but this is questionable). Their report is fairly comprehensive with a few weaknesses (see comments below), but overall not bad. Novelty is not too intriguing but seems acceptable.

Comment 1: Reporting on outcome is inferior and should either be omitted (most likely) or much improved.

Reply: Omitted.

Comment 2: Median 8.5 months of FU is too short to show any impact of grading on survival: this should be clearly indicated; especially also in the conclusion; death is not a short-term outcome in NET-patients, so this information is meaningless and could be cause for misinterpretation of the data; in my opinion, the authors should either try to get much better follow-up data or just indicate that follow-up is too incomplete to report. There is enough data out there to show the relation between grading and survival.

Reply: Modified as suggested .

Follow up duration was inadequate to derive any meaningful conclusion on long/medium term outcomes in our study patients.

Comment 3: Status of lymph node metastasis in these patients (interesting, since LN-metastasis is the the most common location for metastasis in NET's)?

Reply: This has been now added in the manuscript as described below;

Status of nodal disease was also noted. Of the 79 patients, 7 had biopsy proven nodal metastasis and 35 had significant nodes on radiological examination. The remaining 37 patients did not have any significant lymph node enlargement.

Comment 4: The discussion needs to be shortened massively (is boring to read): there is no reason to repeat all the results (clinical presentation, interesting cases, granulomas, comparison of MVI, age, gender in different stage tumors, etc.); this can be discussed without repetition or omitted from the discussion at all. It does not make sense to discuss differences between groups that are very small and are likely chance findings.

Reply: Many of these are deleted and the rest are now shortened in the discussion.

Comment 5: The issue of MVI needs to be toned down: I am lacking a statement that most evaluations came from biopsies, which cannot be viewed as good diagnostic tests to evaluate MVI (is more a chance finding). This is the likely explanation that lower grade tumors (G1) have more MVI than higher grade tumors. Also, in a study only examining metastatic tumors to the liver, I would expect most of the lesions to have MVI. -I am lacking the comparison for MVI between primary tumors and metastasis, where available. I think this would be interesting.

Reply: A statement now has been added regarding MVI and presence of MVI in pathologically proven primaries.

Reviewer's code: 00053419

The authors provide a comprehensive study of neuroendocrine neoplasms of liver that includes 79 patients, some interesting cases among them.

Comment 1: The heterogeneity of the population studied should be taken into account.

Reply: Of the 79 patients, 71 were of Indian origin, 7 from Bangladesh and 1 from Srilanka. This has been now included in the revised manuscript.

Comment 2: The results are clearly exposed but additional discussion would be appreciated to further interpret the coincidence or discrepancy with the studies performed by other authors.

Reply: Some additional discussion has been added but there are not many similar studies to compare.

Comment 3: An overall conclusion at the end of the discussion would be also acknowledged.

Reply: This has been now added as the last paragraph in the revised manuscript.