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**Manuscript NO:** 39863

**Title:** Neuroendocrine Tumor Incidentally Detected During Living Donor Hepatectomy: Two cases treated with complete response

**Reviewer's code:** 03294293

That's a well written manuscript. the subject of the manuscript is interesting. it should be published.

**Response to the Reviewer** (03294293)

Thank you for your valuable comment about our manuscript.

**Reviewer's code:** 2860663

Akbulut and colleagues presents a case-report describing two cases of incidental NETs found During Living Donor Hepatectomy. The topic of the study is interesting. However, it presents some critical points that need to be addressed, as following:

Major Points

- 1) It is not clear which is the aim of this paper, since it is initially presented as a case report. Nevertheless, the authors dedicated a limited space to case report description and follow-up of the two cases is absent. On the contrary they present an extensive description of the natural history and management of the NETs. Finally, they claim to provide conclusions on management of incidental NETs. This is not possible, since a case report cannot provide sufficient evidence to reach conclusions. I believe that the authors should limit themselves to present the two cases, extending the case report section, presenting the follow-up, greatly limiting the narrative description of NET natural history and management (it is not a review of the topic). Finally, every suggestion can only be presumptive, and have to be stated with caution, since sufficient evidences to support definitive conclusions are absent.
- 2) The authors referred a large experience in liver donor hepatectomy. They should present the data of their series, report how many interventions they have done in order to clarify which is the overall prevalence of incidental tumors.



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- 3) The meaning of the title is not clear. There is no answer to the question “What to do?” The have to change it with a descriptive title. For instance: “Neuroendocrine Tumor Incidentally Detected During Living Donor Hepatectomy: two cases treated with complete response”.
- 4) The abstract is not well written and it contains unnecessary details of the two cases that are already provided in the main text (the aim of the abstract is not to substitute the main text).
- 5) The language quality is poor and an extensive revision by a native speaker is essential.

#### Minor Points

- 1) What were the indication to the two transplant? HBV decompensated cirrhosis? Hepatocellular carcinoma? This must be described.
- 2) In both cases, which radiological examinations were performed before the operation? After the intervention, have radiologic images been reviewed to clarify if the two tumors were missed or not at imaging?
- 3) Did the authors found other incidental tumors at preliminary screening before surgery? If yes, which was the incidence of other tumors incidentally found before surgery on radiological examinations?
- 4) Do the authors perform surgical abdominal exploration, routinely? What are possible complications of this procedure? How many adverse effects secondary to this procedure have the authors observed in their series of surgeries?

#### **Response to the Reviewer (2860663)**

##### **For Major Points**

- 1) You are absolutely right. We can not give strong messages from case reports. Our goal here is to create an awareness.
- 2) So far, we have not encountered any incidental tumors during the preoperative donor candidate examination or during living liver donor hepatectomy procedure except this two cases. we found hemangiomas with a diameter of 1-1.5 cm in only one or two donors.
- 3) According to your suggestion, title of manuscript revised
- 4) Abstract section was revised



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5) English language was revised by person who expertise on english language

#### **For Minor Points**

- 1) As we mentioned on the manuscript text, Recipient of first case have chronic liver disease secondary to Hepatitis B Virus infection. Recipient of second case have chronic liver disease+ hepatocellular carcinoma secondary to Hepatitis B Virus infection
- 2) Before 2014, we routinely used multidetector computed tomography (MDCT) to evaluate the abdominal cavity of the living liver donor candidate. But for the last 4 years, we have evaluated all living liver donor candidate with both MDCT and dynamic liver MR/MRCP.
- 3) No. So far, we have not detected any tumoral lesions during preoperative radiological examinations of any living liver donor candidate
- 4) We wrote our suggestion about this issue at the end of the discussion. To be honest, we were not routinely exploring the abdominal cavity during donor hepatectomy for the last one years. In patients who have recently undergone laparotomy for living donor hepatectomy, we have an inspection after the abdominal wall has been upturned with the retractors. Sometimes we are gently palpating the abdominal cavity with powder-free gloves. A prospective study was performed in our clinic to measure the length of the bowel in living liver donors. As far as I have observed, some of these cases have had some problems with gastrointestinal discharge in the early postoperative period.

#### **Reviewer's code: 00503561**

This is an important case reports and the author raise and address the issues to solve in the community. Ki-67 index of NET are proposed in many organs in sometimes different context especially in the lower range, and the evidence so far is far from robust in any conclusions. The outcome of these G1 tumors in the immunosuppressed conditions is unknown. 1. Is it possible to stop the transplantation when incidental high-grade tumors discovered in the operation?



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**Response to the Reviewer (00503561)**

Thank you for your so valuable comment about our manuscript. As you know, there are many publications in the literature about liver transplantation in NET cases. However, there is no data on the use of a liver graft obtained from a living liver donor with neuroendocrine tumors. But deceased donor-derived neuroendocrine tumor. But, two or three case reports on the use of Deceased donor-derived hepatic neuroendocrine tumor have been published. But this is quite different from the events we present in this study. this latest situation arises from the fact that dead donors have not been examined radiologically enough. This is a very difficult question and a difficult decision. According to us, transplantation can be performed if no lesions are detected by peroperative ultrasonography in the harvested liver graft.

**Reviewer's code: 00187828**

The manuscript entitled "Neuroendocrine Tumor Incidentally Detected During Living Donor Hepatectomy: What to do it?" has been evaluated as follows; The authors present two cases with grade 1 neuroendocrine tumors (NET) during living donor hepatectomy (LDH). In the first case during an abdominal exploration revealed that the appendix vermiformis had a 8-10 mm tumor which was removed. In the second case a mass lesion with a 10 mm in size on the antimesenteric surface, approximately 90 cm proximal to the ileocecal valve was detected. A wedge resection with primary closure was performed. The pathological examinations of the specimens of both patients revealed a grade 1 NET [NSE (+), Chromogranin (+), Synaptophysin (+) and Ki 67 (+)]. In conclusion, the authors suggest that even if patients undergoing LDH are healthy individuals, whole abdominal cavity should be gently palpated and all findings be recorded after completing laparotomy. Suspected masses or lesions should be confirmed by frozen section examination. Such an approach would avert some future potential medicolegal issues. The language should be polished.

**Response to the Reviewer (00187828)**



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You have summarized very well what we want to discuss you in this article. Thank you very much for your comments.

With Best Wishes