

Peer Review File

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Reviewer A:

Line 39: Based on reading, it appears that a biopsy was performed before obtaining dedicated cross sectional imaging (CT; PET). Can you clarify why a biopsy was obtained in lieu of a Liver Protocol MRI?

Response 1: Initial workup and biopsy was performed at an outside facility before referral to our institution. We have made changes to lines 37, 45, 50 for further clarification

149: or -> for; Is there any open data series to discuss comparing complications and length of stay

Response 2: to our knowledge, there is no open data series in cases involving liver resection likely due to its rarity.

Overall very interesting

Reviewer B:

Line 6: I suggest to use a better definition of what paraganglioma is, instead of a tumor arising from paraganglia.



Response 3: We have revised the definition of paraganglioma in line 5-6 and revised the statement regarding primary hepatic paraganglioma in line 6.

Lines 10 and 39: I guess that you mean “percutaneous liver biopsy” with the aid of an imaging modality.

Response 4: statements have been revised to indicate “percutaneous liver biopsy”

Line 12: “Possible” primary sites.

Response 5: Revised in line 15

Line 13: Computed tomography of which part of the body? Please specify.

Response 6: Body regions are added on line 14 and 53.

Lines 37, 42, 43: Please add normal values in parentheses.

Response 7: normal values now added

Line 47: It will be interesting if you have a preoperative (ultrasonography) or intraoperative figure to add. I know that this may be impossible.

Response 8: Preoperative ultrasound added to images. There are no saved intraoperative ultrasonography images.

Line 96: “He expressed being grateful for the care received”. This phrase must be omitted.

Response 9: Phrase omitted.

Line 97: Please add histological images.



Response 10: now added to Fig 2

Lines 130-133: “He did have an isolated hypertensive event at the time of biopsy. This combined with the elevated serum metanephrines, allowed us to ensure that he was adequately alpha-blocked prior to his procedure”. You must mention this event in case presentation. It demands more analysis. The patient was on atenolol (beta blocker) and hydrochlorothiazide (diuretic) during the last ten years. In which way the patient was adequately alpha-blocked prior to the procedure? Which is the role of alpha-/beta blockage preoperatively? The hypertensive crisis during percutaneous liver biopsy preoperatively is a serious condition. It means that you could have major cardiovascular complications intraoperatively (even patient’s death) during tumor’s handling and during carbon dioxide insufflations. Please read the following article: “Undiagnosed paraganglioma; a challenge during laparoscopic retroperitoneal resection. Heinze A, Nikomanis P, Petzold F, Rassweiler JJ, Goezen AS. Arch Ital Urol Androl. 2019;90:297–298”. I believe it will help you.

Response 11:

Our institution was notified of the details surrounding his biopsy related hypertensive crisis after his transfer. We appropriately referred him to endocrinology for preoperative optimization. See lines 45, 49, 61 for revisions to address the above questions.

Lines 137-140: “Laparoscopic approach can be challenging for resection of retroperitoneal paragangliomas given the posterior location limiting exposure, the anatomic variations, rich vascularization and the potential for hemodynamic instability due to manipulation”. I guess that you mean the pure laparoscopic technique and not robot-assisted laparoscopic approach. Please read the following article: “Katsimantas,



A., Paparidis, S., Filippou, D., Bouropoulos, K., Sr, & Ferakis, N. (2020). Laparoscopic Resection of a Non-functional, Extra-adrenal Paraganglioma: A Case Report and Literature Review. *Cureus*, 12(4), e7753. <https://doi.org/10.7759/cureus.7753>". It is true that robot-assisted laparoscopic procedures have a lot of advantages in comparison to pure laparoscopic technique. However, robotic platform is not available in health system of many countries. In this case, the patient can still undergo a minimally invasive procedure. Pure laparoscopy presents a lot of well-established advantages compared to open procedure and is cheaper than robot-assisted laparoscopy. The main factor affecting the result of any operation is surgeon's skills, so an experienced, well-trained, skillful laparoscopic surgeon can accomplish retroperitoneal tumor's excision even in the absence of the robotic platform. In any case, the tumor's size, location, degree of vascularization, proximity/adhesions to major vessels and surrounding tissues, and loco-regional invasion may guide the decision to perform each approach.

The figures and figure legends must be modified. You have to use more shapes in each figure to demonstrate what is described in each legend and you should rephrase the legends.

Response 12: Agree with the above. Robotic resection in the discussion refers to robotic assisted laparoscopic approaches in comparison to pure laparoscopic approaches which we have simply stated as laparoscopic in our paper for simplicity. Figures and figure legends have been modified for accuracy.

Reviewer C:

This is an interesting unusual case particularly in its presentation as a hepatic mass and the positivity of (IHC) CD117 which could be identified in only 2-3% of paragangliomas.



- Useful comments of the feasibility and the safety use of robotic resection of retroperitoneal paragangliomas even for tumors which are large or adherent to major vessels and avoiding crisis of catecholamine hypersecretion.

- In introduction: "Paragangliomas make up 22% of pheochromocytomas and are usually benign". The distinction between "benign" and "malignant" paragangliomas has been debated. Currently, all paragangliomas are believed to have some metastatic potential and are assigned malignant tumors by the WHO Classification of Endocrine Organs (2017, 4th edition). Therefore, the previous categories benign and malignant paragangliomas have been eliminated. Please check this issue.

Response 13: The specification as benign has been removed.

- Regards your patient, the diagnosis of paraganglioma was established by preoperative biopsy with an evidence of hypertensive event at the time of biopsy and accompanied with elevation of serum metanephrines, the new recommendation is to prepare all patients with

elevated metanephrines or catecholamines, regardless of symptoms, by administration of preoperative alpha-adrenoceptor blockade for 7–14

days with or without combination by Beta adrenoceptor blockade. Preoperative hydration and liberal salt intake are advisable to avoid hypotension after tumor resection.

Please, what about the vital signs during the surgery in the intraoperative approach.

Response 14: alpha and betablockade were given preoperatively. This is indicated in line 61, 72



- In discussion paragraph you mentioned that mediastinum is a common location for paraganglioma, then you mentioned that unusual sites of origin include mediastinum.

Please check this.

-Line 55 (a upper): (an upper)

- Line 86 (Fib 1d) = (Fig 1d)

- Line 148-149: "Overall, it allowed or the minimally..." . Please check this again.

Response 15: The suggested changes have been made. See lines 59, 89, 156

