Dear editor,

Thank you for your giving us an opportunity to revise our manuscript! Now we are submitting the revised manuscript entitled "Pancreatic paraganglioma with multiple lymph node metastases found by spectral CT: A case report and literature review" for consideration for publication in ***World Journal of Clinical Cases.***

Reviewer 1:

This is a case report on pancreatic paraganglioma with multiple lymph node metastasis in a young patient. Although this case report is interesting, there are several concerns to be mentioned.

Comment 1. Although it is difficult to differentiate pancreatic paraganglioma from other hyper-vascular tumors such as pNETs, the authors have stated that early filling of the drainage veins may be a crucial imaging feature for pancreatic paraganglioma. Why is early filling of the drainage veins formed in patients with pancreatic paraganglioma? Is this finding specific for pancreatic paraganglioma? Isn't this finding observed in patients with pNETs including pNET G3?

Response 1: Formation of the tumor draining vasculature is supposed to depend on a variety of growth factors secreted from the tumor itself [1]. Most pancreatic paragangliomas seem to have a characteristic to induce abundant draining veins, although details of the mechanism of the vessel induction remain to be elucidated. This finding was not specific for pancreatic paraganglioma.

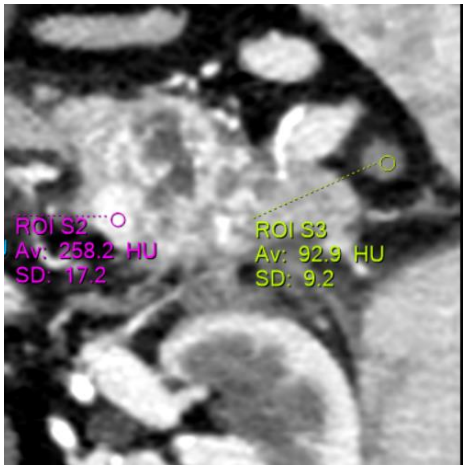
[1]Ruddell A, Croft A, Kelly-Spratt K, Furuya M, Kemp CJ. Tumors induce coordinate growth of artery, vein, and lymphatic vessel triads. BMC Cancer 2014; 14: 354 [PMID: 24886322 DOI: 10.1186/1471-2407-14-354]

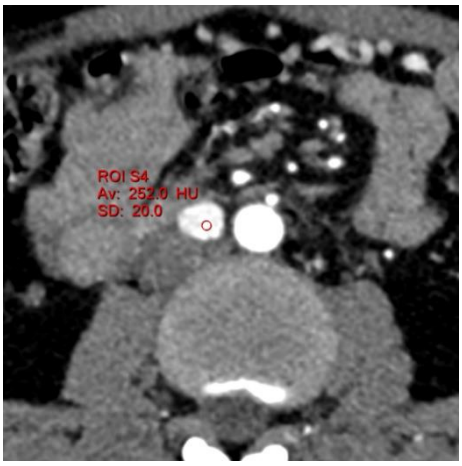
Comment 2. In Figure3, it is difficult to distinguish the spectral curves of tumor (purple) and LN2(red).

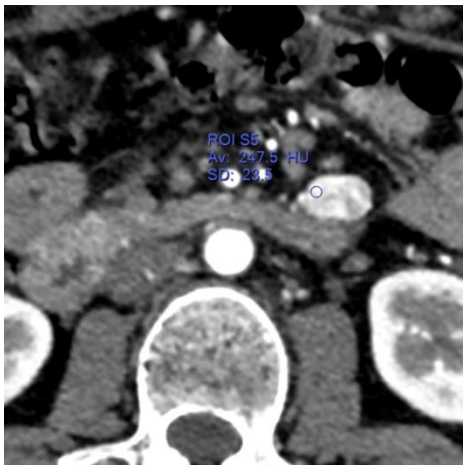
Response 2: In Figure3, the spectral curves of tumor (purple) and LN2(red) partially overlap, so it is difficult to distinguish。

Comment 3. The location of LN1,2, and 3 is unclear in the figures.

Response 3: The location of LN1（yellow）,2（red）, and 3（blue） is shown in the figure. We don't think it's necessary to show these figures in the manuscript.







Comment 4. Post-operative findings of LN 1,2, and 3 should be presented clearly.

Response 4: Thank you for your comments and suggestions! LN2 and 3 are metastatic lymph node confirmed by pathological examination, and we added the description in Figure 3.

Comment 5. Immunological examinations should be included in Figure4.
Response 5: Thank you for your advice! The immunological examination was tested by another institution. The pathology department did not provide us with figures of the immunological examinations.

Reviewer 2:

Specific Comments to Authors: Dual energy post-processing offers advantages over conventional CT in the evaluation of pancreatic mass-like lesions. There is limited data assessing the utility of dual energy CT for pancreatic paraganglioma. Thus it is justified to publish this manuscript eventually. The points are generally clear except the written English needs to be improved by a reputable native English speaker. I have a few points the authors might consider incorporating in the final form.

Comment 1. Given the significant overlap between paraganglioma and pNETs regarding features of histopathological characteristics, lesion heterogeneity, and vascularity, I doubt that the radiological findings report here are specific to pancreatic paraganglioma. Please comment on DLCT features (if there is any) to differentiate paraganglioma from pNETs or solid pseudopapillary neoplasms.
Response 1. There are very limited data assessing the utility of dual energy CT for pancreatic paraganglioma. DLCT has comparable efficacy to conventional CT in differentiating paragangliomas from pNETs or solid pseudopapillary tumors. Compared to conventional CT, DLCT has advantages in assessing pancreatic tumor borders, degree of invasion, and lymph node metastasis.

Comment 2. The gold standard for diagnosis of pancreatic mass still relies on pathology examination. In a young female patient with a large vascular-rich pancreatic mass nonfunctioning pNET and solid pseudopapillary neoplasm are the top differential diagnoses. I was surprised to see EUS-FNA or EUS-FNB was not utilized for preoperative evaluation in both hospitals. A touch print or smear from the tumor would reveal classical features of a neuroendocrine tumor. Sudden spikes in blood pressure and heart rate during EUS-guided FNA of unexpected paragangliomas or pheochromocytomas can be managed. Granted that paragangliomas can have endocrine degenerative atypia, the lack of mitotic figures in proportion to nuclear atypia should lead the pathologist away from rendering a diagnosis of high grade malignancy. What is "mucinous spindle cell soft tissue tumor?" I was more troubled by the aggressive treatment based on an erroneous pathology diagnosis or no definitive diagnosis when the mass was not even life-threatening.

Response2. Before being transferred to our hospital, it is very unfortunate that the patient was misdiagnosed twice at two different hospitals and received aggressive treatment protocols. The reason why neither hospital utilized EUS-FNA or EUS-FNB for preoperative evaluation is not clear to us. The pathological examination showed a mucinous spindle cell soft tissue tumor, which we were also very puzzled about.

Comment 3. Page 6 pathology description: change "cuboidal cells" to "polygonal cells" change "supporting cells" to "sustentacular cells" "endomysial (EMA)" is wrong. Please change to "epithelial membrane antigen (EMA)" The authors described pathology findings with some errors and showed a figure depicting H&E stained pancreatic paraganglioma, but made no effort to include a pathologist as a coauthor or at least to acknowledge the pathologist's contribution, unless the pathologist did not want to be included.

Response3. Thank you for your advice. We have revised the typos throughout the article. The pathologist did not want to be included as a coauthor and we acknowledge the pathologist's contribution in the manuscript.

Comment 4. I assume that blood pressure levels and heart rates were not significantly altered during the procedures and there were no plasma/urine levels fractioned metanephrines and catecholamines measured. If so, please state in the manuscript. Page 4: two blood glucose levels mentioned. When were those two levels measured? Was the blood glucose level normalized after the surgical procedure? TPO-Ab level was high. When was it measured? Could it be related to previous immunotherapy or directly associated with paraganglioma? Was the level normal after the surgical procedure?
Response 4. Thank you for your comments and suggestions！We added the description in Laboratory examinations and TREATMENT. The first laboratory examinations on admission showed that the patient's fasting glucose and antithyroid peroxidase antibody (TPO-Ab) were 9.03 mmol/L and 359.88 IU/ml ,neither of which returned to normal after surgery.。Elevated TPO-Ab levels may be related with immunotherapy.

Comment 5. Genetic testing and counseling to this young patient is needed. Plasma chromogranin may be attempted for patient followup.
Response 5. Thank you for your suggestions！We will recommend these measures to patient.

Comment 6. Page 2 CASE SUMMARY: please change "8.0 cm in length" to "8.0 cm in greatest dimension." End of page 4: "7.1 cm x 3.7 cm x 6.7 cm" to "7.1 cm x 6.7 cm x 3.7 cm" Page 5 TREATMENT: "10 cm" inconsistent with 7 to 8 cm mentioned Figure 3: "Pancrease" to "Pancreas"
Response 6. Thank you for your reminding. We have amended the error.

Round 2

Dear Editors and Reviewers: On behalf of my co-authors, we thank you very much for giving us an opportunity to revise our manuscript, we appreciate editor and reviewers very much for their positive and constructive comments and suggestions on our manuscript entitled "Pancreatic paraganglioma with multiple lymph node metastases found by spectral CT: A case report and literature review" (No.78910). We have studied reviewer's comments carefully and have made revision which marked in red in the paper. We have tried our best to revise our manuscript according to the comments. Attached please find the revised version, which we would like to submit for your kind consideration.

Comment 1. End of section of Chief complaints: delete the last sentence since the grammar is wrong and the finding was described in the following section

Response 1: Thank you for your comments and suggestions! We have deleted the sentence.

Comment 2. Section of History of present illness: change "and showed a tendency toward a mucinous spindle cell soft tissue tumor" to "with the diagnosis of mucinous spindle cell soft tissue tumor favored."

Response 2: Thank you for your advice. We have made correction according to the Reviewer's comments.

Comment 3. Section of FINAL DIAGNOSIS: delete "and CD34" since the tumor cells are negative for CD34 and CD34 stain only highlights endothelial cells within the tumor. Change "incisal" to "excisional" or "resectional" since "incisal" is a typo and incision refers to cut into part of the tumor.

Response 3: Thank you for your reminding. We have amended the error.

Comment 4. Section of TREATMENT first line: change “above” to “imaging” since the surgery was performed after imaging finding but not after the diagnosis. I would suggest the authors label the pages and lines so that it would be much easier for a reviewer to comment on the manuscript.

Response 4: Thank you for your comments and suggestions! We have made correction according to the Reviewer’s comments. We are very sorry to say that after consulting with the pathology department, we were unable to obtain the figures containing scale bars with number. Thank you and best regards. Yours sincerely, Corresponding author: Name: Kang Li E-mail: lkrmyydoctor@126.com