

Dear editor and reviewers:

Thank you very much for the comments and suggestions. We've made appropriate changes in the revised manuscript according to your suggestions. Followings are answers to each detailed question.

Reviewer #1:

1) Line 55: Please present the size of tumor in all three dimensions.

I've revised and presented the size of tumor in three dimensions in the manuscript.

2) Line 56: Is it in the body OR tail of the pancreas?

The tumor is more close to the tail of the pancreas so I revised the "body and tail" to "tail"

3) Line 99: "and" -> "or"?

I've revised in the manuscript.

4) Line 102: remove "a case of"

I've revised in the manuscript.

5) Line 142: remove "observed"

I've revised in the manuscript.

6) Line 205: spell author's name properly (Chick?).

I've revised in the manuscript.

7) Line 212: Should there be a reference by Vilana et al.?

Yes, I've added the reference in the manuscript.

Reviewer #2:

1. The author provided an informed consent for surgery rather than informed consent for publication. If informed consent for publication is not feasible for this patient, an alternative way is to get an IRB approval. Since the image in the case report did not contain any personal information, in most institute, investigator could get institution IRB approval for case report with waive of informed consent.

We had an informed consent for publication and got ethics certificate of approval, as follows:



山东省立医院 医患协议书

姓名： 年龄： 72 岁 科室： 东院消化内科 住院号：

尊敬的患者及家属：

衷心感谢你们的信任，选择到我院就医，为了进一步密切医患关系，保证正常的医疗秩序，请医患双方自觉遵守以下协议：

一、患者的权利和义务

1. 患者享有隐私权、知情同意权、自主医疗权等；患者有权选择诊治医师，有权了解自己的病情，检查项目、治疗方法、医疗风险和预后等事项；患者在进行或拒绝手术及其他特殊检查治疗时，必须签署书面知情同意书。2. 患者有权监督医院的工作可随时对医疗服务、医院管理等提出意见或建议。对违反医院规章制度的医务人员实事求是地向医院反映举报。3. 患者不准向医务人员送“红包”贵重礼品，共创廉洁和谐的医疗环境。4. 患者应遵守医疗秩序和医院的规章制度：应尊重医护人员诊治权；应积极配合诊疗活动，如实提供病史等信息，尊重科学，对疾病诊断治疗中客观存在的危险做出慎重理智的决定。5. 患者有按时交纳医疗费用的义务。住院时要交纳规定数量的医疗预交金，住院期间医疗费用超过预交金时，必须及时补交。出院时次结清，不得拖欠。患者有权知晓医疗费用的使用情况。6. 患者入院实行实名制，住院期间保管好自己的钱财及贵重物品，不得私自离开病房。7. 患者应尊重医务人员爱护公共设施，服从管理和安排。发生医疗异议时，应当依法解决。不得干扰我院正常的医疗秩序，不得侵犯医务人员的人身安全。对违反上述规定的患方人员，医院将予以教育、劝阻，不听劝告者后果自负。必要时通知有关部门处理。

二、医务人员的权利和义务

1. 医务人员在医疗活动中应秉持平等、仁爱、诚信的职业精神，严格执行医疗卫生法律、行政法规、部门规章和诊疗护理常规。2. 医务人员要充分履行告知义务，尊重患者知情权等各项权利。用清晰、易懂的语言如实向患者或代理人告知患者病情治疗原则、诊疗方案、医疗风险以及预后等，告知患者诊疗活动中各种用于检查的组织、体液等也可能会用于以服务人类健康为目的的科学研究。3. 医务人员应保护患者隐私权，执行保护性医疗措施。4. 医务人员应以患者为中心，尽心尽责治疗疾病。不断提高医疗水平，严防差错事故的发生。5. 廉洁行医，不以医谋私，不得接受患者及其家属的“红包”、贵重礼品。6. 医务人员应文明行医，态度和蔼，仪表端庄，举止文雅：应用文明用语，禁止使用服务忌语，不断提高服务意识。7. 医务人员有权拒绝患方的不合理要求。

对违反上述规定的医务人员，医院将按有关规定进行处理。

同意 ☒ 不同意 ☐

2024.12.11

ETHICS CERTIFICATE OF APPROVAL

(NO. SWYX2023-010)

PROJECT TITLE	Percutaneous transhepatic intraportal biopsy using a gastroscope biopsy forceps for diagnosis of a pancreatic neuroendocrine neoplasm: A case report		
PRINCIPAL INVESTIGATOR	Qian Ding	INSTITUTION /DEPARTMENT	Department of Gastroenterology, Shandong Provincial Hospital Affiliated to Shandong First Medical University
FUNDING	National Natural Science Foundation of China, No. 82000566. Natural Science Foundation of Shandong Province, No. ZR2020QH036. Natural Science Foundation of Shandong Province, No. ZR2022MH010		
DOCUMENTS	1. Ethics Review Application; 2. Research Program; 3. Informed Consent; 4. Resume of Principal Investigator; 5. Certificate of authenticity of case history		
REVIEW CONCLUSION		APPROVED	
1.This approval applies to research ethics issues only. 2.The approval does not obligate an institution or any of its departments to proceed with activation of the study. 3.The approval is required before research can commence. 4.The approval will automatically invalid if the project do not start within 6 months.			
Biomedical Research Ethics Committee of Shandong Provincial Hospital 2023-01-16			



2. If possible, please provide the gross picture of the specimen obtained from forcep biopsy. It will help readers to get further insight about this procedure.

I added the gross picture of the specimen obtained from biopsy forceps in Figure S1.

3. The diagnosed of grade 2 NET is based on mitotic count and Ki-67. It will be better to provide the pathology image of Ki-67 in Fig 3. If there is no enough space for Ki-67 photo, please remove one of IHC (chromogranin A or synaptophysin)

I've revised in the manuscript according to your suggestion.

Reviewer #3:

1. Specific comments Line 105: How do you find gastric varices without an image or endoscopy on a physical exam?

I'm sorry for the improper depiction, actually the patient underwent an endoscopy and I've

revised in the manuscript.

2.Line 108: better to say pancytopenia

I've revised in the manuscript.

3.Line 138: Avoid using a trade name for octreotide

I've revised in the manuscript.

4.What was the reason for using gastroscope biopsy forceps rather than a needle which is usually used for the IR approach?

For the location of tumor in this case is in the extrahepatic main portal vein trunk and splenic vein, it is unavailable for transhepatic puncture approach with needle. Also, due to the existence of gastric varices, it is unsafe to get the biopsy by approaches through gastric wall either under the guidance of endoscopic ultrasound or CT.

Regarding the reason of using a biopsy forceps rather than a needle through the sheath from the portal vein is as follows: 1) we did not have a biopsy needle longer than the vessel sheath. 2)the biopsy forceps is easier to control. 3) the biopsy forceps could get larger tissue than needle each time.

5.The author made a comparison to EUS-FNA. Does Reference 23 include other approaches that could be potentially safer?

As we mentioned in the manuscript, we performed similar work as in Reference 23 did, we consider both of our work were safe. As mentioned in reference 23, "In conclusion, this series of transvenous biopsy of intravascular and perivascular masses suggests that it is a safe and accurate procedure for tissue sampling and can easily and spontaneously be performed in the context of many interventional procedures", our work also support their conclusion.

6. Is gastroscope biopsy forceps sterile? We typically do not place this into a sterile environment, which is within the vasculature, so this reviewer is not familiar with sterility. I am unsure if this is a good fit for the WJ gastro as the primary readership is for a gastroenterologist who usually does not perform this procedure. Better fit for case report journal or interventional radiology journal.

The gastroscope biopsy forceps we used were sterile, we also confirmed with manufacturer that it could be placed into a sterile environment.