

Answer reviewers #1

1. The BMI could be a factor which can affect the risk of neuroendocrine factor, it would be more professional to mention the BMI of the patient in the manuscript, and any weight changes as well.

Answer: Because the patient was 26 weeks pregnant and his body weight was significantly higher than that when he was not pregnant, BMI did not mention it, but it was recorded in the hospital admission record. 56kg, 1.58m, body mass index (BMI) 22.4 kg/m².

2. Smoking history and drinking history are other important factors in pancreatic carcinoma, did the authors check drinking and smoking history before the pregnancy or not?

Answer: The patient had no history of smoking or alcohol consumption.

3. Mentioning blood characteristics (WBC count, platelet count) more specifically at the time of the first admission and after the treatment, could help other scientists and improve the citation of the paper.

Answer: An initial blood test of the complete blood count (white blood cells count, 18.86*10⁹/L, hemoglobin level, 76 g/L, platelet count, 163*10⁹/L).

4. providing a table with features of the most recent reported pNETs cases (e.g., 2000-2019) during pregnancy would be more helpful to the reader and improve citation.

Answer: Complete the table file "2000–2019 pNENs in pregnancy review article".

Answer reviewers #2

Questions:

1. Dose viral hepatitis markers, such as HBs antigen or anti HCV, were checked in this patient? Is there any sign of cirrhosis in the initial study of abdominal ultrasonography? Elevated Alpha fetoprotein (AFP) value (179.60 ng/mL) was found in this patient. Is elevated AFP related to pregnancy or HCC?

Answer: Viral hepatitis markers in this patient were negative. Elevated AFP was related to pregnancy and multiple metastatic lesions in the liver.

2. Although the pictures of abdominal CT were presented, there was no sequential change could be traced. Readers could not compare the pictures before treatment with those pictures after treatments. Moreover, the initial abdominal ultrasonography (US) pictures should be shown because abdominal US was the first tool to detect the liver tumors.

Answer: There had have sequential changes could be trace. I chose CT with significantly smaller lesions post-treatment for comparison. There was no sign of cirrhosis in the initial study of abdominal ultrasonography in emergency.

3. The description in the section of physical examination was crude. For example, if abdominal distention was detected, abdominal shiftiness

sound (percussion examination) should be recorded because ascites might develop when portal hypertension (portal vein thrombosis).

Answer : The physical examination had no abdominal shiftiness sound. Because the patient had no ascites.

4. Please explain the meaning of elevated tumor markers, such as AFP, CA125 and CA199 in this patient. Was chromogranin A (CaA) checked in this patient?

Answer: Immunohistochemical staining of the biopsy revealed that the tumor cells were positive for CgA (Figure 2.).

5. In the section of treatment, “The patient underwent transcatheter arterial chemo-embolization three times” was recorded. For a patient with portal vein thrombosis (especially main portal vein thrombosis), TACE is risky to induce hepatic failure. The author should explain why TACE was chose as a treatment for this patient. And why Sandostatin (octreotide acetate microsphere, 30 mg) but not systemic chemotherapy or targeted drugs was prescribed for this patient?

Answer: Somatostatin analogue (SSA) has the effect of hormone symptom control and anti-tumor proliferation. It is a common first-line treatment choice for patients with well-differentiated GEP-NET in the late stage recommended by domestic and foreign guidelines. If the first-line treatment of SSA progresses, the addition of SSA can further prolong the progression-free survival time of the patients, or combine other treatments such as targeted therapy and chemotherapy on the basis of SSA according to the different conditions of the patients.

The treatment of pNENs complex liver metastasis is based on systemic medication, including somatostatin analogues, targeted drugs and chemotherapy, which can inhibit hormone secretion and anti-proliferation, but the overall objective response rate (objective response ratio, ORR) is not high. Interventional therapy via hepatic artery can safely and quickly reduce the load of liver tumor and hormone secretion, and there are many options for significantly improving ORR, SSA combined therapy, each of which has its own advantages and disadvantages. How to identify the potential beneficiaries of combined therapy, realize individualized treatment and improve the long-term survival of patients is an urgent problem to be solved.

6. The content of discussion is detail and informative, but it should be correlated with this case report. If the clinical presentation or treatment was not consisted with the guideline or general rules, author should explain the difference. For example, in the discussion section, “The sensitivity of gallium 68Ga-PET-CT is higher than that of 18F-FDG-PET-CT in determining staging of pNETs[34,35]” was reported. But 18F-FDG-PET-CT was used in this patient. “

Answer:My hospital dosen't have ⁶⁸Ga-PET-CT.

Answer reviewers #3

I suggested that title of the manuscript can be changed as "Pancreatic neuroendocrine carcinoma in a pregnant woman: A case report and literature review". - Keywords should be selected according to MeSH. - Introduction is small; please specify importance of pNETs diagnosis in pregnancy and its clinical outcomes. - The method of reaching a definitive diagnosis and how to eliminate other possible diagnoses should also be carefully described in the case presentation section more clearly. - Dear author, this interesting Case report needs some clarification regarding the discussion part - maybe to make a comparison table regarding your case vs published cases you mention in the discussion, with all characteristics and treatment approach, duration of treatment and outcomes.

1. The title of the manuscript has been changed as "Pancreatic neuroendocrine carcinoma in a pregnant woman: A case report and literature review".
2. The part of discussion in article has also been carefully described the method of reaching a definitive diagnosis, how to eliminate other possible diagnoses and how to treat.
3. Complete the table file "2000–2019 pNENs in pregnancy review article".

All these revisions have been mentioned in the 62607-manuscript.