Response to Reviewer:

Reviewer Name: Anonymous

Review Date: 2022-10-22 00:23

1. Differential diagnosis. The author describes how protein-losing enteropathy and various infections were suspected as the patient's diagnosis. Have the following three diseases with anaemia, abdominal pain, diarrhoea and weight loss also been considered? The first is pellagra. The patient had a history of heavy alcohol consumption and may not have had good nutritional status. Did the patient have a niacin deficiency?

RESPONSE: Yes, appreciate reviewer's comments. In terms of differential diagnosis, we also considered the three diseases you mentioned at the beginning of diagnosis and ruled out them. When we learned that the patient had anemia, abdominal pain, diarrhoea, and weight loss, we also performed vitamin B3 testing. We added this test results as follows: In addition, the vitamin B3 level was 17.1 ng/ml, which was within the normal range. (Page 6, line 120-121, in red)

2. Second, lead poisoning. At the time of the initial examination, was it checked, for example, whether the patient worked with lead-acid batteries?

RESPONSE: Yes, the patient's family was interviewed, and he had no history of exposure to lead-acid batteries or related occupational exposures before admission. At the same time, we know that lead poisoning can stimulate the increase of reticulocytes in humans, and lead to hemolysis, renal dysfunction, neurological symptoms, etc. In contrast, the reticulocyte count was $45.50*10^9$/L, and the reticulocyte ratio was 1.12%, and these results were negative. The total bilirubin level was 12.0 μmol/L, the direct bilirubin level was 4.9 μmol/L, the indirect bilirubin level was 7.1 μmol/L, the creatinine level was 63.1 μmol/L, and the glomerular filtration rate was 134.76 ml/min/1.73m^2), which were all within the normal range. (Page 6-7, line 119-123, in red). In addition, this patient did not have convulsions or delirium before or after admission, so we did not consider this disease.

3. Third, porphyria. Although this disease is relatively rare, it should be considered in the differential of patients with unexplained gastrointestinal symptoms.

RESPONSE: Thank you very much for your valuable advice. We know that porphyria is a kind of disease caused by the lack of enzyme activity in the heme biosynthesis pathway, which causes abnormal increase in the concentration of porphyrin or its precursors and accumulation in tissues, resulting in cell damage. The clinical manifestations are mainly skin photosensitivity, hyponatremia, and neuropsychiatric symptoms, accompanied by changes in urine color. However, our patient had only gastrointestinal symptoms and a normal urine color, so we also ruled out this disease.

4. Treatment. The author describes that the patient eventually died due to rapid leukaemia. What could have caused the patient's rapid leukaemia?

RESPONSE: We appreciate the advice sincerely. However, allow me to point out a small mistake on your part. In our manuscript we mentioned that this patient did not die of acute leukaemia, but of acute leukopenia. The first SMILE regimen was performed from August 1, 2021 to August 4, 2021. On the first day of chemotherapy, the patient had diarrhea and developed hematochezia once, approximately 50 g. However, the symptoms of diarrhea, abdominal pain, and hematochezia were relived on the second day of chemotherapy. The patients stayed in the hospital until August 10, 2021, when he improved uneventfully

without leukocytopenia (white Blood Cell count, 5.05*10^9/L). Unfortunately, two days after discharge, he died from leukopenia and severe septic shock in a local hospital. (Page 9, line 177-183, in red).

5. And was the patient treated with G-CSF preparations such as naltograstim?

RESPONSE: We did not treat this patient with a G-CSF preparation. The proof is as follows: The hematologist kept him under observation after chemotherapy, and the symptoms of diarrhea, abdominal pain, and hematochezia were relived on the second day of chemotherapy. The patients stayed in the hospital until August 10, 2021, when he improved uneventfully without leukocytopenia (white Blood Cell count, 5.05*10^9/L). (Page 9, line 180-183, in red).

6. Palliative care The authors indicate that Intestinal NKTCL is a disease with a poor prognosis. Has appropriate palliative care been provided for the patient and his family?

RESPONSE: Yes, for palliative care, after the patient was admitted to the hospital, we continuously supplemented human serum albumin 10g bid for 10 days for hypoproteinemia. At the same time, the patient had obvious abdominal pain, so we gave pinaverium bromide for spasmolysis and pain relief, and at the same time, we gave negative air ion therapy to improve the patient's immunity. Pneumatic therapy was administered to prevent thrombosis. At the same time, we also actively encouraged patients to cooperate with treatment, so as to avoid patients falling into depression.

Reviewer Name: Anonymous

Review Date: 2022-10-28 09:30

1. We acknowledge the significance of EUS-FNB and MFCI, but it is not one early diagnosis method and it can't provide assistance for early diagnosis.

RESPONSE: Thank you for pointing out the mistakes in our article in time. In view of our mistakes, we make the following corrections: the sentence "In light of the lack of understanding of the disease, early diagnosis and treatment are particularly crucial." has been changed as "In light of the lack of understanding of the disease, diagnosis and treatment are particularly crucial." (Page 11, line239-240, in red)

2. How to calculate ki-67 proliferation index? and what's the formula?

RESPONSE: Thank you very much for your question, the formula of calculating ki-67 proliferation index is: ki-67 proliferation index= The number of Ki67 positive cells/ Total number of tumor cells**.**

3. The legend of figure 4 is not expressed clearly. The result of it should not appear in the figure legends, and the subfigure should be explained accurately.

RESPONSE: Thank you very much for your valuable comments, we have revised the relevant information and put them in the appropriate position and explained the subfigure accurately. (Page 8, line161-164, in red, and Page 16-19)

4. In the line 26-28, please pay attention to the position of punctuation mark after two funding numbers and the former should be a comma.

RESPONSE: Yes, according to your precious advice and the request of the journal, we changed "Supported by Major Science and Technology Project of Zhejiang Provincial Department of Science and Technology (No. 2020C03030). And the Foundation of Zhejiang Educational Committee. (No. Y202146136)" to "Supported by Major Science and Technology Project of Zhejiang Provincial Department of Science and Technology, No. 2020C03030, and the Foundation of Zhejiang Educational Committee, No. Y202146136." (Page 2, line 26-28, in red)

5. In the line 50, Replace the word "treatment" with "treatments".

RESPONSE: Thank you for advice on precise wording. We changed the word "treatment" to "treatments". (Page 3, line 48-49, in red)

6. In the line 57-58, the word "its" should be deleted and "...for improving the ...and reducing the...will be better.

RESPONSE: Thank you for your valuable advice. We deleted the word "its" and changed "Some key factors, including EUS characteristics, the right choice of FNB needle, and its combination with MFCI, are crucial for the improving the diagnostic rate and the reducing the misdiagnosis rate." to "Some key factors, including EUS characteristics, the right choice of FNB needle, and combination with MFCI, are crucial for improving the diagnostic rate and reducing the misdiagnosis rate." (Page 3, line 53-55, in red)

7. Key words: we suggested that the "pancreatic cancer" should be deleted.

RESPONSE: Yes, we have deleted the "pancreatic cancer" in the part of "Key words". (Page 3, line 56-57)

8. In the line 130-131, two "were" should be modified to "was".

RESPONSE: Thank you for advice on precise wording. The sentence "there were circular

solid-occupying lesions in the pancreatic head that were 88 *47*52 cm in size." has been changed to "there was a circular, solid-occupying lesion in the pancreatic head that was 88 *47*52 mm in size." (Page 7, line 132-133, in red)

9. In the line 137, "cholangiopancre atography" should be one word and linked.

RESPONSE: Yes, we changed "cholangiopancre atography" to "cholangiopancreatography". (Page 7, line 136, in red)

10. In the line 144, the word "to" after "ALP" can be deleted.

RESPONSE: Thank you very much for your precise advice, we deleted the word "to" after "ALP". (Page 7, line 143, in red)

11. You have written multicolor flow cytometry immunophenotyping with the abbreviation MFCI in the line 69. You should also use the abbreviation MFCI in the line 157, 163 and 223.

RESPONSE: Yes, we have changed the "multicolor flow cytometry immunophenotyping" of three revised places you mentioned into the abbreviation "MFCI". (in red)

12. In the line 165-166, "hematologist consultation" should be corrected with appropriate form.

RESPONSE: Yes, "hematologist consultation" has been changed to "advice from consulted hematologists". (Page 8, line 165, in red)

13. In the line 189, "a distinct ethnic and regional distribution" should be modified to plural form.

RESPONSE: Yes, we changed "a distinct ethnic and regional distribution" to "distinct ethnic groups and regional distributions". (Page 9, line 191-192, in red)

14. In the line 192, please delete a "only" after "for".

RESPONSE: Thank you very much for your careful advice, we have deleted the "only" after "for". (Page 9, line 194)

15. In the line 198-200, please correct the grammar of the sentence.

RESPONSE: Yes, the statement of the sentence is not accurate. It was revised as: They noted that inflammatory cell infiltration is the most common factor that delays the diagnosis of NKTCL[9]. In the differential diagnosis process of NKTCL, PET-CT can not only provide standard images but also help accurately stage the disease [10-12]. (Page 9, line 200-203, in red)

16. In the line 200, please correct the grammar of "PET-CT can not only image standardly...".

RESPONSE: Thank you for advice on precise grammar. It was revised as: PET-CT can not only provide standard images but also help accurately stage the disease (Page 9, line 202-203, in red)

17. In the Figure 1 legends part, please correct the unit "cm".

RESPONSE: Yes, appreciate reviewer's comments. We have changed the unit "cm" to"mm" in the Figure 1 legends part. (in red)

Reviewer Name: Anonymous

Review Date: 2022-11-01 11:06

1. Title. While the location of the lesion is in proximity to the head of pancreas, the clinical findings and previous imaging approaches to establish the diagnosis of head of pancreas mass are inconclusive. I may find the statement 'mimicking pancreatic cancer' is a bit exaggerating.

RESPONSE: Yes, thank you for your constructive comments. The statement 'mimicking pancreatic cancer' is a bit exaggerating. Therefore, we changed the title to"Intestinal natural killer/T-cell lymphoma presenting as a pancreatic head space-occupying lesion: A case report ". (in red)

2. Abstract. The presented information in abstract, especially in the case summary, is a bit too redundant.

RESPONSE: Yes, we made revision of the "case summary" according to the valuable advice as follows: In this case, we introduce a male who presented to the clinic with edema of both lower limbs, accompanied by diarrhea, and abdominal pain. Endoscopic ultrasound (EUS) showed well-defined homogeneous hypoechoic lesions with abundant blood flow signals and compression signs in the head of the pancreas. Under the guidance of EUS- fine needle biopsy (FNB) with 19 gauge (19 G) or 22 gauge (22 G) needles, combined with multicolor flow cytometry immunophenotyping (MFCI) helped us diagnose NKTCL. During treatments, the patient was prescribed the steroid (dexamethasone), methotrexate, ifosfamide, L-asparaginase, and etoposide (SMILE) chemotherapy regimen. Unfortunately, he died of leukopenia and severe septic shock in a local hospital. (Page 3, line 43-51, in red)

3. Background. While NKTCL may occur in any segment of intestinal tract, its distinct location at periampullary, of which leading the clinicians to the 'mimicking head of pancreas mass', should also be addressed.

RESPONSE: Yes, your valuable advice should be added in the "Background": While NKTCL may occur in any segment of the intestinal tract, its distinct location in the periampullary region, which leads clinicians to consider mimics of a pancreatic head mass, should also be addressed. (Page 3, line 38-40, in red)

4. Case presentation. The previous CT finding of 'edema and thickening of the small bowel wall', without mentioning any enlarging mass at the head of pancreas and or dilation of the biliary tree or pancreatic duct, may, at least, provide a clue of otherwise head of pancreas masses, in addition to irrelevant clinical and laboratory findings. While the most current work up diagnostic approaches were more convincing, as the disease seemed progressing.

RESPONSE: Yes, thank you for your recognition of our past work. Through this case we also learned that EUS-FNB with a 19 G or 22 G biopsy needle combined with MFCI could be a good choice for diagnosis and for subtyping lymphoma.

5. Discussion. I compliment the authors for providing the complete diagnostic work up before the diagnosis of NKCTL was made. I got an impression of the highlight of the diagnostic work up, from inconclusive yet leading to diagnosis of CT and MR imaging, PET-CT, and EUS, tissue sample retrieval by endoscopic US and FNB, to histopathology and IHC of which eventually leading to the diagnosis of NKCTL. Despite the eventually mortal prognosis of the disease in general, the earlier manifestation of the disease should raise a

concern. From the information presented by the authors, I may find a sense of delayed definitive diagnostic work up, and thus, disease treatment. I think the choice of chemotherapy should also be discussed.

RESPONSE: Yes, appreciate reviewer's comments. We discussed the choice of chemotherapy in the discussion: Presently, in the course of NKTCL treatment, asparaginase-containing chemotherapeutic schemes are the standard treatment regimen [19]. Based on previous experience, SMILE is the most popular regimen for the treatment of NKTCL[20]. In a study of 87 NKTCL patients treated with the SMILE regimen, for newly diagnosed stage III/IV patients, the complete response rate was 40%-54%, and the 5-year overall survival rate was 47%[21]. (Page 10-11, line 230-235, in red)

6. Illustrations and tables. I found the numbering of images is not in order and confusing, without any corresponding captions available.

RESPONSE: Thank you for your valuable advice, we have placed the pictures in the corresponding numbered position of each picture and explained the subfigure accurately. ((Page 8, line161-164, in red, and Page 16-19))

7. Units. Please correct the typo on the size unit (mm instead of cm).

RESPONSE: Yes, appreciate reviewer's comments. We have changed the unit "cm" to"mm" .(in red)

EDITORIAL OFFICE'S COMMENTS

I recommend the manuscript to be published in the World Journal of Gastrointestinal Oncology. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: https://www.referencecitationanalysis.com/.

RESPONSE: Thank you very much for your valuable advice. We have accessed the RCA database and cited the relevant literatures according to the methods you provided.