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IMPACT FACTOR 8

Peer Review File

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Reviewer A:

Comment 1: It is well known that a significant fraction of patients with pancreatic cancer exhibit high levels of IgG4. So I do not think this case is rare. Type 1 AIP often manifests as a paraneoplastic syndrome. Unfortunately, the autors have not addressed this point.
Reply 1: Thanks for your professional comment; indeed, type 1 AIP, especially mass-forming type, often shares many similar characteristics with pancreatic carcinoma. Considering that EUS, accompanied by biopsy, provides localized examination, only a surgical specimen pathology can definitively determine whether it represents a mimicry or a complication, like the patient we reported. However, such determination is crucial for evaluating prognosis and choosing subsequent treatment strategies. Consequently, even for patients diagnosed with type 1 AIP, heightened vigilance and rigorous follow-up are essential when any signs suggestive of malignancy emerge to prevent potential misdiagnoses. Thanks for your comment again.
Changes in the text: We have added some discussion about this question in the revised manuscript (see Page 3, lines 9 to 16).

Reviewer B:

This paper described a rare case of pancreatic cancer coexisting with type 1 autoimmune pancreatitis. The case is of interest and the paper is generally well-written. I have some comments as described below.

Comment 1: As you know, type 1 autoimmune pancreatitis is a pancreatic manifestation of systemic IgG4-related disease, so wasn't there any multiorgan involvement?
Reply 1: Thanks for your detailed comment; we carefully reviewed all records and examinations of the patient; in addition to the pancreas, her gallbladder and bile duct were also involved: 1) her abdominal ultrasound, CT, and EUS all revealed the following changes, including an enlarged gallbladder with wall thickening, dilated intra- and extra-hepatic bile ducts, dilated common bile duct with wall thickening, and stenosis of the distal common bile duct; 2) the pathological examinations of surgical specimens suggested chronic cholecystitis with apparent chronic inflammation of bile duct wall.
Besides, her CT examination showed that lymph nodes distributed in the mediastinum, hilus of the lung, and right cardio-phrenic angle were plump and enlarged, and some of them represented by groups 4R, 5, and 7 had slightly higher radioactive uptake in PET/CT with SUVmax 3.7. Thus, the possibility of involvement is not excluded.
Changes in the text: We have added the above-detailed information to the revised manuscript (see Page 2, lines 30 to 32, Page 2, line 44, and Page 3, line 1).

Comment 2: Please specify the serum CEA and DUPAN-II levels.

Reply 2: Thanks for your kind reminder. As for the serum CEA, the patient was tested only once during the first visit to the local hospital in December 2022 with 4.80 ng/ml (normal limits: <=5.00 ng/ml). After that, during the visit to our hospital, she underwent serum CEA tests three times with 4.9 ng/ml, 4.1 ng/ml, and 2.8 ng/ml, respectively. Overall, her serum CEA levels were stable and below the normal limits.

Regarding DUPAN-II, as the precursor substance of CA19-9, it has been thought of as a potential biomarker for pancreatic cancer with a sensitivity of approximately 70%. And its role is primarily of being complementary to identifying pancreatic cancer patients with negative CA19-9 caused by negative Lewis. However, this biomarker is still in the research phase, and most are small cohorts with a limited number of patients that need more high-quality evidence-based medical evidence. Additionally, DUPAN-II is not part of the routine in our center; hence, we apologize for not being able to provide this data.

Changes in the text: We have briefly described the serum CEA of this patient in the revised manuscript (see Page 2, lines 7 to 8).

Comment 3: Were the findings of IgG and IgG4 staining in the initial EUS-FNA specimen supportive of type 1 autoimmune pancreatitis?

Reply 3: Thanks for your professional comment. The EUS-FNA of this patient you mentioned was completed at the local hospital, and they did not perform IgG and IgG4 staining. It is a pity that we had difficulty obtaining this sample for additional immunohistochemistry; thus, we could only use the information provided by the local hospital. As we described in the manuscript, the pathology of EUS-FNA demonstrated that histocytes were the predominant components, with a small number of lymphocytes, whereas no atypical cells were found, and Ki-67 was negative. Hence, it was more inclined to be a chronic inflammation than a neoplastic disease.

Changes in the text: We have added those details in the revised manuscript (see Page 2, lines 17 to 18).

Comment 4: Please provide details of the puncture needle used for EUS-FNAB.

Reply 4: Thanks for your professional reminder. The initiate EUS-FNA of this patient was undergone at the local hospital, and we do not know the details of the needle. As for the later EUS-FNB at our hospital, we used 22G Acquire^{TM} Endoscopic Ultrasound Fine Needle Biopsy (FNB) Device (Boston Scientific, Marlborough, MA).

Changes in the text: We have modified our text as advised (see Page 2, lines 37 to 38).