Response to reviewer 1

Comments to the auther:

This paper reports the pathology of a case of ampullary papilloma. The pathological result is a special type, and the disease is rare in the world. The pathological type of ampullary tumor was IMPC. The logic of the whole article is very good, and the author correctly judged the pathological type of the tumor. The article describes a rare case, which is slightly less novel. The article has the following problems.

Thank you for your valuable suggestion. In accordance with the comments received, we have added some information about the patient's present illness, personal and family histoly, physical examination, laboratory data and regimen of adjuvant therapy. Moreover, we have described a suggested etiology of ampullary carcinoma in the patient using previous reports. We have amended the scale of CEA (line 8, page 7) to ng/mL from mg/mL.

1. The author followed up the patients for 6 months, and no abnormality was found in the follow-up results. Some authors pointed out that the median survival time of these patients was 11 months, so please pay close attention to the changes of patients. Special treatment methods or drugs will affect the survival of patients, which will have important significance for future patients. List the treatment plan of patients during 6 months after operation.

We have added a brief statement on the treatment plan of the patient during the 6 months after surgery in the Treatment and Outcome and Follow-Up sections, as described below.

TREATMENT

The patient underwent subtotal stomach-preserving pancreatoduodenectomy with D2 lymphadenectomy. He received chemotherapy after surgery with oral administration of S-1 (also known as TS-1; Taiho Pharmaceutical Co. Ltd.; Tokyo, Japan). The initial dose of S-1 was determined according to the body surface area and administered at 80 mg per day. A 2-week administration followed by a week rest was continued as postoperative adjuvant chemotherapy for a year.

OUTCOME AND FOLLOW-UP

The postoperative course showed abdominal pain caused by the pancreatic fistula,

which was successfully treated with fluid replacement and fasting for 7 days. The patient was discharged 21 days after surgery. The patient received postoperative chemotherapy as described above and was monitored at regular intervals through clinical examinations, biochemical investigations, and imaging studies.

2. Some data are listed in the laboratory examination. Are these data before or after treatment? If it is the data before treatment, what is the result after chemotherapy?

The laboratory examination was performed before treatment. We have added the data on serum tumor marker levels of CEA and CA19-9 after surgery in the Outcome and Follow-Up section.

One month after the surgery, the serum CEA level was 4.1 ng/mL and CA19-9 level was 15 U/mL, both of which were lower than those before surgery. However, 6 months after the surgery, serum CEA levels increased gradually, whereas CA19-9 levels remained normal (Figure 4).

3. The author suggested that the patient received chemotherapy after operation. Please explain the specific drug and cycle of chemotherapy.

The patient received S-1 (also known as TS-1; Taiho Pharmaceutical Co. Ltd.; Tokyo, Japan). The initial dose of S-1 was determined according to the body surface area and administered at 80 mg per day. A 2-week administration followed by a week rest was continued as postoperative adjuvant chemotherapy for a year.

4. In the last sentence of the discussion, the author said that the patient has no other tumors, and ampullary carcinoma is the primary tumor. Therefore, it is very important to analyze the possible causes of ampullary carcinoma in the discussion. In addition, the author did not mention whether the patient had a history of smoking.

We have also included a hypothesis explaining how ampullary carcinoma occurs, as described below.
Most cases of ampullary adenocarcinoma develop sporadically. Cigarette smoking and chronic infection by *Fasciola hepatica* are considered risk factors; however, our patient reported smoking a cigarette at the age of 20, although very briefly. Neurofibromatosis type I, familial adenomatous polyposis, and Muir–Torre syndrome seem to be

predisposing factors for ampullary carcinomas, but these syndromes were not observed in the present case.