

Dear Dr. Ying Dou

Thank you for your consideration of our manuscript (47006), and we thank the reviewer for the helpful comments. Enclosed please find the revised manuscript, the changes in which are described in our point-by-point responses to the reviewers' comments below.

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Point-by-point responses to the comments of Reviewer 1

1. Why was the diagnosis of hematoma entertained at first presentation? Was there any history of blunt trauma or anticoagulant medication use? In the presence of a solid tumor, would have been better to proceed with further EUS and surgery at first presentation.

⇒ We have explained the patient's medical history as follows:

- Before: She underwent computed tomography of the abdomen and pelvis at another hospital and was transferred to the out hospital. Contrast-enhanced computed tomography scan revealed poorly enhancing heterogenous mass adjacent to the anterior wall side of the gastric lower body (Figure 1A). A perigastric abscess or hematoma or gastric submucosal tumor (SMT) was suspected at that time, and she was hospitalized. The patient underwent sonography for percutaneous drainage insertion after admission and had a focal hypoechoic solid-like lesion with an internal echogenic component on the anterior wall side of the gastric antrum, but there was no evidence of an internal cystic lesion, suggesting that the hematoma was the most suspicious (Figure 1B). She was treated with antibiotics, tranexamic acid, proton pump inhibitor and conservative therapy. She was discharged from the hospital and was followed up from an outpatient clinic.

- After: The patient had no specific history of past illness such as trauma or medication. Due to abdominal pain 1 year prior, she underwent computed tomography (CT) of the abdomen and pelvis at another hospital and was transferred to our hospital. A contrast-enhanced CT scan revealed a poorly enhanced heterogenous mass adjacent to the anterior wall of the gastric lower

body (Figure 1A). A perigastric abscess or hematoma or a gastric submucosal tumor (SMT) was suspected at that time because the patient had mild fever, abdominal pain, and a poorly enhanced heterogenous mass, and was hospitalized. The patient underwent sonography for percutaneous drainage insertion after admission and a focal hypoechoic solid-like lesion with an internal echogenic component on the anterior wall of the gastric antrum was found, but there was no evidence of an internal cystic lesion, suggesting that the hematoma was suspicious rather than an abscess because a small amount of blood component had drained (Figure 1B). She was treated with antibiotics, tranexamic acid, a proton pump inhibitor, and conservative therapy. Because her symptoms improved, the patient was discharged without any further examination (such as endoscopic ultrasound) and underwent regular follow-up in the outpatient clinic. (line 4, page 5 of the revised version)

2. Is there a better image on EUS, showing all layers of gastric wall intact with the tumor outside the gastric wall ? or the distinction between a sub-mucosal vs extra-gastric lesion could not be made due to attenuation of the layers?

⇒ We have changed the EUS image to one that shows all layers of the gastric wall, as follows:

- Before: Endoscopic ultrasonography was then performed, and the findings were a heterogeneous hypoechoic mass of approximately 6.73 × 2.75 cm in size (Figure 1E). Endoscopic ultrasonography-guided fine needle biopsy (EUS-FNAB) was performed, but the tumor was not diagnosed histologically; thus, a surgical resection was planned.

- After: EUS was performed next, and the findings were a heterogeneous hypoechoic mass of approximately 6.35 × 3.00 cm that appeared similar to a gastric SMT of fourth layer origin (Figure 1E). EUS-guided fine needle biopsy (EUS-FNAB) was performed due to suspicion of a gastric SMT based on the EUS findings, but because the tumor was not diagnosed histologically, surgical resection was planned. (line 13, page 6 of the revised version)

3. It is not clear from the description of surgery whether a part of gastric

wall was excised along with the tumor or the tumor could be separated from the stomach?

⇒ We have revised the manuscript as follows:

- Before: Although the mass was severely adhered to the wall of the stomach, the stomach was preserved by excision after mass dissection using a Harmonic scalpel.

- After: Although the mass strongly adhered to the wall of the stomach, the tumor was able to be completely separated from the stomach by harmonic scalpel dissection, and the stomach was completely preserved without abstinence. (line 24, page 6 of the revised version)

Minor point. The description of IHC in Discussion can be shortened.

⇒ We have revised the manuscript as follows:

- Before: Histopathological and immunohistochemical exams are tools to help with differential diagnosis. According to the meta-analysis of Chortie et al, calcification, inflammatory cells, and dense hyalinized collagen in the histopathological examination of CFT were almost 100% defined by the disease definition^[4]. Immunochemical staining is helpful for differential diagnosis, mainly Vimentin and Factor XIIIa staining^[4, 11, 12]. This case confirmed that Factor XIIIa is positive and CD34, SMA, CD117, and B-catenin are negative. This case required discrimination from gastric SMT, and immunochemical staining also helped in this evaluation. First, CD17 and CD34 are helpful for GIST^[6, 13-16].

- After: Pathologically, calcification, inflammatory cells, and dense hyalinized collagen are characteristic of CFT, as is immunohistochemical staining for vimentin and Factor XIIIa staining^[4, 11, 12]. This case required discrimination from gastric SMT, which was facilitated by immunochemical staining. CD117 and CD34 are helpful for distinguishing CFT and GIST^[6, 13-16]. (line 24, page 8 of the revised version)

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Point-by-point responses to the comments of Reviewer 2

1. Page 6, last paragraph: 'First, CD17 and CD34 are~~~' should be corrected as 'First, CD117 and CD34 are~~~'.

⇒ We apologize and have corrected the error.

- Before: First, CD17 and CD34 are helpful for GIST

- After: CD117 and CD34 are helpful for distinguishing CFT and GIST (line 27, page 8 of the revised version)

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Point-by-point responses to the comments of Reviewer 3

1. Please discuss about differential diagnosis including solitary fibrous tumor, inflammatory myofibroblastic tumor, and IgG 4-related disease et al.

⇒ We have added some discussion and revised the manuscript as follows:

- Before: Histopathological and immunohistochemical exams are tools to help with differential diagnosis.

Desmin and SMA are useful for distinguishing leiomyoma[7]. Immunochemical staining is helpful for differentiating from inflammatory myofibroblastic tumor, which is difficult to distinguish[3, 12-14, 16-18]. IMT is also positive for SMA and ALK-1. In some cases, CD34, CD68, IgG, and IgG4 may be partially expressed[4]. Larson et al. have suggested that this may be an IgG4-related disease, but this should be further studied[4, 19]. Therefore, in this case, IgG4 was not examined.

- After: For diagnosis, CFT must be differentiated from various other types of tumors. The most important differential diagnoses in intra-abdominal CFT are GIST, leiomyoma, inflammatory myofibroblastic tumor (IMT), solitary fibrous tumor, and IgG4-related disease. Due to their heterogenous symptoms, these

tumors are diagnosed based on imaging and pathologic findings, including immunohistochemical staining. (line 19, page 8 of the revised version)

Desmin and SMA are useful for distinguishing leiomyoma^[7]. Inflammatory myofibroblastic tumor (IMT), which is difficult to distinguish from CFT, is positive for SMA and ALK-1^[3, 12-14, 16-18]. Solitary fibrous tumors have a hypercellular component, a heterogenous pattern of spindle cells, and are positive for CD34, CD99, and bcl-2. In some cases, CD34, CD68, IgG, and IgG4 may be partially expressed^[4]. Larson et al. suggested that CFT may be an IgG4-related disease, because it shows a histopathologic pattern of dense lymphoplasmacytic infiltration, fibrosis, and obliterative phlebitis^[4, 19]. However, this idea requires further investigation because Chortie et al. reported that fewer than 10 cases exhibited positive IgG4 staining^[4]. Unfortunately, in the present case, IgG4 was not assayed. (line 1, page 9 of the revised version)

2. Were there any cases of calcifying fibrous tumor originating from the gastrohepatic ligament in the literatures?

⇒ We searched for instances of CFT in Medline and Embase but did not find any cases originating from the gastrohepatic ligament. Because we therefore think that this is the first such report, we have revised the manuscript as follows:

- After: Furthermore, no report of CFT of gastrohepatic ligament origin was found in the literature; therefore, this may be the first case report. (line 9, page 8 of the revised version)

We have also corrected numerous minor errors.

Thank you for your time.

Faithfully,

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