

Feb. 16, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name:16295-review.doc).

Title: Diagnostic Utility of EUS-FNA for Glomus Tumor of the Stomach

Authors: Shin Kato, Kaoru Kikuchi, Kenji Chinen, Takahiro Murakami, Fumihito Kunishima

Name of Journal: World Journal of Gastroenterology

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Revision has been made according to the suggestions of the reviewers

Reviewer No.2670768

<Major>

(1) I recommend that three following cases would be added to the review: 1) Mohanty SK, et al. Diagnosis of gastric glomus tumour by endoscopic ultrasound-guided fine needle aspiration cytology: a case report. *Cytopathology*. 2014;25(3):205-7. 2) Matevossian E, et al. Glomus tumor of the stomach simulating a gastrointestinal stromal tumor: a case report and review of literature. *Case Rep Gastroenterol*. 2008;2:1-5 EUS-FNA was not successful 3) Akahoshi K, et al. Clinical usefulness of endoscopic ultrasound-guided fine needle aspiration for gastric subepithelial lesions smaller than 2cm. *J Gastrointestin Liver Dis*. 2014;23(4):405-12 One case was included.

We have added the three cases recommended by reviewer. Additionally, we updated Table1 to add a review of these three cases and have changed the following text in the discussion.

In the eight reported gastric glomus tumor cases, FNA (EUS-FNA in seven cases, percutaneous FNA in one case) was performed preoperatively for pathological diagnosis ^[15, 16, 18-23]. Table 1 shows the clinical characteristics of those eight cases, as well as our case. In seven cases, a correct preoperative diagnosis was achieved from EUS-FNA specimens, whereas two cases were misdiagnosed as a neuroendocrine tumor or GIST. In the misdiagnosed cases, FNA specimens were not subjected to IHC analysis ^[19, 23].

(2) In introduction, the author described “we report a case of small glomus tumor of the stomach”. The tumor was 3.0cm in diameter. Was it small as glomus tumor of the stomach?

As you have noted, the tumor size in this case (3.0cm) was not very small. This is supported by a literature review of glomus tumors of the stomach (Kanwar et al.) that reports the average size of a glomus tumor of the stomach to be 2.7cm. We have deleted the word “small” from the text of introduction.

(3) It may be difficult to perform EUS-FNA for an intramural solid tumor smaller than 1cm technically, and there is a risk of needle penetration and seeding of malignant cells. On the other hand, the malignant case was reported that the size of tumor was less than 1cm (Reference 4). What is your diagnostic and therapeutic algorithm for SMT of the stomach?

We have added the following explanation to the text of discussion.

In cases of small SMT, it is rather difficult to obtain specimens by EUS-FNA, and the procedure carries the risks of needle penetration and malignant cells seeding. However, Akahoshi et al. reported the safety of EUS-FNA for gastric SMTs smaller than 2cm after performing EUS-FNA in 90 cases without complication ^[18]. EUS-FNA for small SMT (<2.0cm) should be performed carefully to prevent needle penetration and seeding, especially in cases exhibiting some malignant characteristics (e.g. necrotic change in the tumor, and rapid growth).

<Minor>

(1) “Uruma-city” to “Uruma” ? In authors contribution, “Kato S collected ...” ?

We have corrected “Uruma-city” to “Uruma”. We deleted “collected the data and ”.

(2) In introduction, references should be added as cases of malignant glomus tumor

We cited four references involving malignant glomus tumor cases in the Introduction.

(3) Fig1 A&B These slices of images seem to be different. Could you show corresponded position slices? ?

This patient underwent plain and enhanced CT examination on different days; therefore, these two images depict the position slices with the best correspondence.

(4) In Table 1, what is the abbreviation of LC?

LC abbreviates lesser curvature. We have defined this abbreviation in Table 1.

Reviewer No.02546401

<Minor>

(1) Could the authors provide more detailed information about the re-examination 36 months after surgery in case report? Could the authors provide the information about the therapy after surgery in case report?

We have added the following information to the case report section.

This patient did not receive any adjuvant therapy after surgery, as no evidence of malignancy was found in the resected specimen. Regular clinical follow up with EGD was performed, and the patient shows no signs of recurrence at 36 months after surgery.

(2) Could the authors provide more detailed experiences or important points during the course of endoscopic ultrasound-guided fine-needle aspiration biopsy in case report?

We have added the following information to the case report section.

We performed EUS-FNA (UCT-240; Olympus Medical Systems, Tokyo, Japan) using a 22-gauge needle (Echotip; Wilson-Cook, NC, USA) while taking care to avoid needle penetration and puncture of the anechoic component of the mass to prevent tumor seeding.

Reviewer No.02676022

<Minor>

(1) In fig 2, 4 there are no quantitation analysis data for positive stained synaptophysin.

We have added the following description to the discussion section. We have also added images of synaptophysin staining as Figs 2 and 4.

The IHC analysis of our case revealed positivity for both muscle actin and synaptophysin. Synaptophysin positivity is occasionally found in specimens from glomus tumors of the stomach, whereas other neuroendocrine markers, including chromogranin A, are generally negative ^[24]. Therefore, we consider these IHC results to be consistent with a glomus tumor.

(2) In Table 1, describe the advantage of 22-gage needle compare to 25-gage needle (Minoda et al) if possible.

We have added the following information to the discussion section.

It remains controversial whether a 22G or 25G needle can adequately obtain a specimen from SMT lesions. Although we selected a 22G needle in this case, 25G needles were used to obtain sufficient specimens in other reported cases. Further analysis regarding needle gauge selection is expected to resolve this issue.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

A handwritten signature in black ink, appearing to read 'Shin Kato', with a stylized flourish at the end.

Shin Kato, M.D.

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