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Professor Damian Garcia-Olmo
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Manuscript for Submission: "Preoperative detection and localization of small bowel hemangioma; two case reports," by Takase *et al.*

ESPS Manuscript NO: 33571

Dear Editor,

Thank you very much for reviewing our manuscript by Takase *et al.* (ESPS Manuscript NO: 33571). We hope that you find our manuscript suitable for publication in *World Journal of Gastroenterology (WJG)* after revision along the reviewers' comments. According to the points raised by the three reviewers, we revised the manuscript as much as we can. The details of the revision and answers for their questions are described in the revision notes. The modified points are indicated in red. We also consulted the KN international professional language editing services to polish up the English of the manuscript. I deeply thank the Editor and you for giving us extra opportunity to improve the manuscript.

Sincerely yours,

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A. Responses to the comments raised by Reviewer (Reviewer's code: 02823555)

Language polishing: "...diagnosed modalities for small bowel hemangioma" consider: "...diagnostic modalities.. "...

We agree with the Reviewer's comment. We revised the indicated grammatical error.

Abstract (page 3, line 2–4), we modified a sentence as indicated in red.

Among the various **diagnostic** modalities for small bowel hemangioma, video capsule endoscopy (VCE) and double-balloon enteroscopy (DBE) can be recommended as part of the work-up in patients with obscure gastrointestinal bleeding (OGIB).

VCE in the accurate diagnosis.." consider: "...in the accuracy of diagnosis and..

We agree with the Reviewer's comment. We revised the indicated grammatical error.

Abstract (page 1, line 4–7), we modified a sentence as indicated in red.

DBE is superior to VCE in the **accuracy of** diagnosis and therapeutic potential, while in most cases total enteroscopy cannot be achieved through only the antegrade or retrograde DBE procedures.

Concerning Case 1, why was resection deemed necessary after successful clipping of the bleeding spot? Was malignancy suspected? ?

Regarding Reviewer's comment, the small bowel lesions with OGIB, especially in over 40 years of age, occasionally potentiate the risk of malignancy. Therefore, we performed a video-assisted laparoscopic enterectomy in addition to endoscopic hemostatic clipping of the lesion.

hyperlipidemia type" what is this supposed to be?

Regarding Reviewer's comment, we revised *Case 2* to correct false notation.

Case 2 (page 6, line 11–12), we modified a sentence as indicated in red.

He had hypertension, **hyperlipidemia** and type 2 diabetes mellitus without complications.

Discussion: ?Gastrointestinal tract-derived bleeding is a life-threatening development“ Consider rephrasing because this sentence is too general and lacks accuracy, e.g. ?Intraluminal gastrointestinal bleeding can be a life-threatening condition“ ?..

We agree with the Reviewer’s comment. We revised the indicated grammatical error.

Discussion (page 7, line 5), we modified a sentence as indicated in red.

~~Gastrointestinal tract derived bleeding is a life-threatening development.~~

Intraluminal gastrointestinal bleeding can be a life-threatening condition.

OGIB is defined as overlooked gastrointestinal bleeding..“ I would not say ?overlooked“ as this indicates something was visible but failed to be recognized. In case of OGIB this is rarely the case when egd and colonoscopy with adequate preparation have been performed. ?..

We agree with the Reviewer’s comment. We revised the indicated grammatical error.

Discussion (page 7, line 5–8), we modified a sentence as indicated in red.

~~Among the various types, OGIB is defined as overlooked gastrointestinal bleeding after a negative initial evaluation using conventional endoscopy including esophagogastroduodenoscopy (EGD), colonoscopy (CS) and radiologic imaging^[5, 6], which often results in a diagnostic dilemma.~~

In case of OGIB this is rarely the case when esophagogastroduodenoscopy (EGD) and colonoscopy with adequate preparation have been performed^[5, 6], which often results in a diagnostic dilemma.

neoplasms, Meckel’s disease and polysosis syndrome.“ Polypsis syndrome? ?

We agree with the Reviewer’s comment. We revised the indicated grammatical error.

Discussion (page 7, line 12–14), we modified a sentence as indicated in red.

In patients under 40 years of age, inflammatory bowel disease, the most common cause, is followed by Dieulafoy's lesions, neoplasms, Meckel's disease and **Polypsosis** syndrome.

VCE can be recommended as part of the routine work-up in patients with obscure bleeding or iron-deficiency anemia[14]“ This sentence is problematic because it could be misinterpreted in a way that all patients with iron-deficiency anemia would require VCE, which is certainly not the case. Please clarify! ?

We agree with the Reviewer's comment. We revised the indicated grammatical error.

Discussion (page 8, line 8–10), we deleted a sentence as indicated below.

VCE can be recommended as part of the routine work-up in patients with obscure bleeding ~~or iron-deficiency anemia~~^[14], and it is not contraindicated except in patients with stenosis of the intestine.

Advanced implementation of VCE including India ink tattooing made the decision of insertion course easy, and the endoscopic process facilitated early treatment, resulting in avoidance of progression to life-threatening status.“ I do not believe VCE directly enables India ink tattooing. Please clarify sentence. What is meant by ?insertion course“? Please rephrase and clarify.

We agree with the Reviewer's comment. We revised the indicated error in sentence.

Discussion (page 9, line 17–19), we modified a sentence as indicated in red.

~~Advanced implementation of VCE including India ink tattooing made the decision of insertion course easy~~ **The preceding implementation of VCE made the selective decision of DBE insertion easy**, and the endoscopic process facilitated early treatment, resulting in avoidance of progression to life-threatening status.

Figure 1 ?The details localization of target lesion using fluoroscopy indicates in the

end of endoscope insertion (arrow) (C). The lesion was underwent endoscopic hemostatic clipping (D).“ Please correct these sentences with the help of a native speaker.

We agree with the Reviewer’s comment. We also consulted the KN international professional language editing services to polish up the English of the Figure legends. We revised the Figure legends (Figure 1, Figure 2 and Figure 3) below.

Figure 1, we revised sentences as indicated in red.

Figure 1 Evaluation of endoscopic findings (Case 1). Video capsule endoscopy (A) and double-balloon enteroscopy (B-C) show a raised lesion with smooth surface in the upper jejunum, and double-balloon enteroscopy ~~shows~~ **showed** a spout bleeding of the lesion. **The lesion in the jejunum was disclosed 29 min after capsule ingestion (pylorus passage at 16 min) (A).** ~~The details~~ **Detailed** localization of ~~the~~ target lesion using fluoroscopy ~~indicates~~ **is shown by** in the end of endoscope insertion (arrow) (C). The lesion ~~was~~ underwent endoscopic hemostatic clipping (D).

Figure 2, we revised sentences as indicated in red.

Figure 2 Surgical and pathological findings (Case 1). ~~Surgical~~ **The surgical** finding on single port laparoscopic surgery shows an objective site with India ink tattooing (A).; Surgical specimen from the small intestine, including the ~~indicated~~ lesion **indicated** with India ink tattooing. Inset shows a whole view of the resected lesion (B). Histological findings (H-E stain) in the resected specimen show ~~a circumferentially proliferated~~ different-sized distended blood vessels **circumferentially proliferated** from ~~the~~ mucosa to submucosa. Inset shows a low-power field view (C).

Figure 3, we revised sentences as indicated in red.

Figure 3 Evaluation of clinical findings (Case 2). Early-phase contrast-enhanced computed tomography reveals small nodule enhancement in the ileum (arrow) (A).; Video capsule endoscopy (B) and double-balloon enteroscopy (C) show a submucosal tumor-like raised lesion with central

erosion in the lower ileum. The lesion in the jejunum was disclosed 145 min after capsule ingestion (pylorus passage at 140 min) (B). Inset indicates the fluoroscopic localization of target lesion in at the end of the endoscope insertion using fluoroscopy (arrow) (C). Surgical specimen from the small intestine, including the indicated lesion with India ink tattooing (D). Histological findings (H-E stain) in the resected specimen show a circumferentially circumferential capillary growth without atypia from the mucosa to the muscle. Inset shows a low-power field view (E).

Please clarify how you were able to use VCE for localization in the Jejunum vs Ileum.

Passage time? X-rays?

Regarding Reviewer's comment, we identified the localization of the lesion using passage time of VCE. We revised the Figure legends (Figure1 and Figure 3).

1. Figure 1 (line 2–3), we added a sentence as indicated in red.

The lesion in the jejunum was disclosed 29 min after capsule ingestion (pylorus passage at 16 min) (A).

2. Figure 3 (line 3), we added a sentence as indicated in red.

The lesion in the jejunum was disclosed 145 min after capsule ingestion (pylorus passage at 140 min) (B).

Please also clarify the role of contrast enhanced imaging vs VCE and DBE. It would be helpful for the clinician if you could propose a diagnostic algorithm.

Regarding the suggestion, we agree with the Reviewers comments and we revised the discussion section.

Discussion (page 9, line 19–22), we added sentences as indicated in red.

In the present case report (*Case 2*), CECT showed small nodule enhancement in the lesion. Therefore, the preceding CECT with a characteristic of rapid and minimally invasive technique may omit VCE, making it a useful algorithm for further early treatment.

B. Responses to the comments raised by Reviewer (Reviewer's code: 02582003)

Some procedure, like the Indian ink tattooing, must be better explained.

Regarding the suggestion, we agree with the Reviewers comments and we revised the Discussion section.

Discussion (page 8, line 19–page 9, line 1), we added sentences as indicated in red.

A previous study reported on colonic tattooing in animal model with various agents, such as methylene blue, indigo carmine, toluidine blue, lymphazurine, hematoxylin, eosin, indocyanine green (ICG) and India ink^[17]. Only ICG and India ink tattoos persisted for more than 48 hours, while ICG was associated with allergic reactions and systemic toxicity^[17]. Therefore, endoscopic marking with India ink is used widely as a visualization technique for colorectal cancer, to define the operative location.

C. Responses to the comments raised by Reviewer (Reviewer's code: 00186781)

Were interesting and useful case report.

We deeply thank the Reviewer and you for giving us extra opportunity to the manuscript.