Nov 12, 2021

Editor in Chief, *World Journal of Clinical Cases*

Dear Editor,

Decision on Manuscript NO.: 71003, Case Report_Revision
**Median arcuate ligamentum syndrome : <mark>4</mark> Case series**

Dear Editor and reviewers;

We thank the Editor and reviewers for their interest in our paper and for their comments, which have helped us to improve the manuscript substantially.

We revised the paper in response to these comments and provided a point-by-point response to the concerns raised by the reviewers.

**Sincerely,**

Poong-Lyul Rhee MD, PhD

Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul, 06351, Korea

Phone: +82-2-3410-3409; Fax: +82-2-3410-6983

E-mail: plrhee@gmail.com

**Reviewers' comments:**

1 Peer-review report

**Reviewer #1: The authors presented 4 cases of MALS successfully managed by medical therapies. The subject is interesting, there are few reports in the literature describing more than one case. However, the manuscript needs a careful review of wording and phrasing by an expert on English language.**

Answer : We also underwent English editing (by Harrisco company, en.harrisco.net) of the revised manuscript. Minor changes in grammar and the correction of typographical errors were not highlighted in this revision. Other than that, all changes have been marked by highlighting in the revised manuscript. Please do not hesitate to contact us if you have any questions related to this paper.

**Additional comments: - Indicate the posology and duration of the treatments administrated. - The patients were treated with different drug protocols (amytriptiline, tegoprazan, gabapentine, meloxicam, famotidine, esomeprazole…). Please outline the reasons to choose one over another in each specific clinical scenario.**

Answer: The first case was a patient who had been using a proton pump inhibitor (PPI) or protective agent for several years, and the diagnosis was confirmed through computed tomography angiography (CTA). Even after using amitriptyline before gabapentin, the visceral neurologic pain improved. This patient had also complained of heartburn with pain. If the symptoms do not improve further after long-term follow-up, adding gabapentin and a painkiller like meloxicam is planned. The second case was a patient who had felt pain for 20 years and and the reason for the long-lasting pain could not be determined, so we immediately focused on pain control agents for the neurologic pain. The third case was a patient who had an alcohol use disorder and visited the emergency room for pain. The prescription was also focused on pain control. And in the fourth case, there was no improvement from PPIs taken before, and pain was the main symptom, so pain control was the treatment focus.

In conclusion, the reason for the marked improvement in median arcuate ligamentum syndrome (MALS) was that neurologic pain was improved by the administration of gabapentin and meloxicam. Treatment with antacids, PPIs, H2 blockers, and potassium-competitive acid blockers (PCABs) did not play a major role, but it was planned to play a protective role against NSAIDs and an adjuvant role with the main component. The first case typically showed improvement by amitriptyline, but the pain intensity was slightly weaker than that in the other cases, so this was a case that might have improved with a drug for functional dyspepsia. In cases 2 through 4, the clinician's judgment indicated that it was highly likely that excruciating pain would not be resolved by an emollient such as amitriptyline. We added the sentence about the patient in the first case (page 4, line 82) (page 5, lines 98-103).

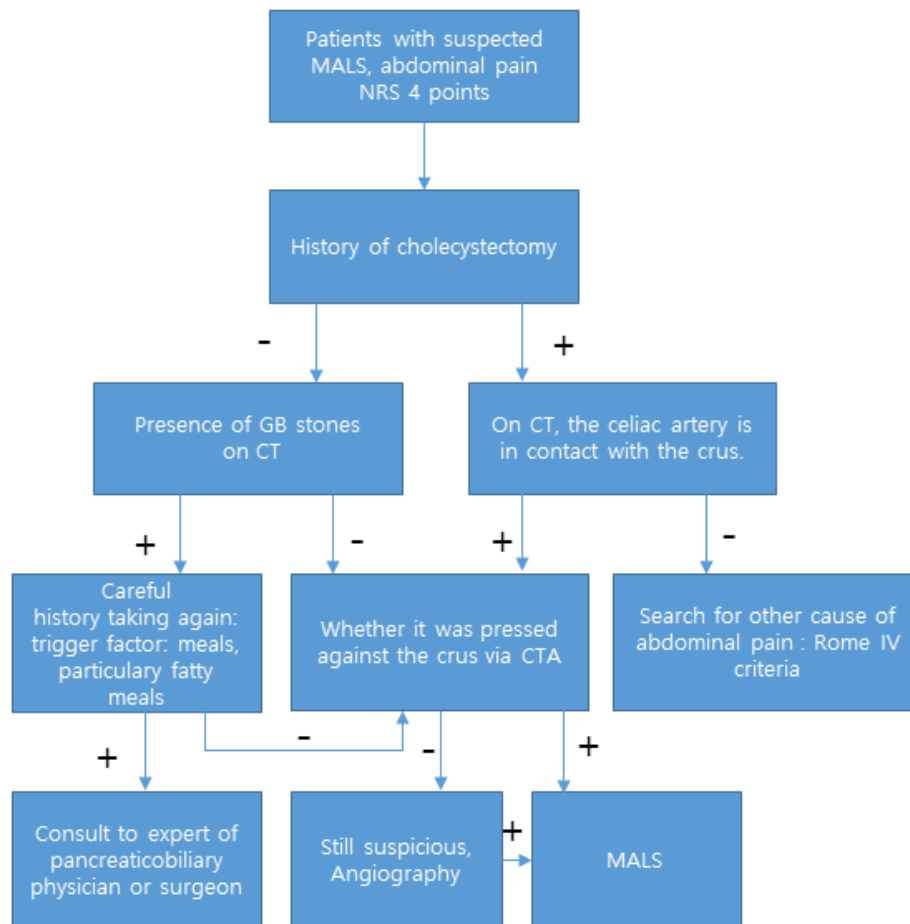"complaining of epigastric pain with heartburn symptoms…"

"The patient showed an immediate symptom improvement response to amitriptyline before active analgesic administration. Thus, even before active pain treatment, through diagnosis alone, improvement was already demonstrated. During follow-up, if any pain remains after observation for more than 3 months, a pain relief agent and an active agent for reducing neurotransmitters will be used. "

**- Indicate the alternative surgical treatments for MALS, together with their expected outcomes based on the literature. - Describe a proposed algorithm to diagnose MALS in patients in which the disease is suspected. State the different imaging alternatives, their typical findings, and state the gold standard exploration to reach a definitive diagnosis.**

Answer: To evaluate whether the celiac artery is in contact with the diaphragmatic crus due to early branching, and whether it is touched or not, an arterial enhanced image, such as thin-slide CT, is required. Therefore, radiologists discuss the CT protocol used for making a diagnosis. However, since the gastroenterologist comprehensively judges all clinical results, it is necessary to evaluate these results after predicting them in advance. We presented the following algorithm and added this content to the Discussion section (page 7, lines 177-179).

"And since the gastroenterologist judges all the clinical results together, the evaluation is performed after confirming these. The following algorithm illustrates

Abbreviations : MALS, Median arcuate ligamentum syndrome; NRS, Numeric pain rating scale; CT, Computed tomography; CTA, Computed tomography angiography

**- Have you planned any additional treatments for the patients not presenting a complete relief of the digestive symptoms?**

Answer: Currently, the goal of surgery is to correct the blood vessels. In fact, since the pain felt by ischemia is not intermittent and not reversible, most of the blood vessels are in contact with the crus, but most of the pain is considered a neurological

symptom. This is because the drug showed an effect, as seen in the four cases. However, people with underlying medical conditions who are taking other medications or taking multiple psychiatric medications may not experience a dramatic effect from medical treatment. And as shown in the first case, for a short period of time, amitriptyline had an effect. In any case, it is possible to combine drug administration before a surgical approach, and this is an area that needs to be studied further and proven. For example, a hospitalized psychiatric patient was suspected as having MALS on CT due to severe pain complaints, but the patient refused to undergo CTA and it could not be proven. If the diagnosis is confirmed after performing CTA, she will need surgery to expect improvement.

**Reviewer #2:** add 4 to title it is a good case series to remind the readers of this syndrome but it needs photographs

Answer: Thank you. We did as you recommended.

**Reviewer #3:** Thank you for this article. It will be good to include in manuscript the information (or algorithm) about "red flags" for MALS - how clinicians can suspect this disease in common practice.

Answer: Please refer to the algorithm in the answers mentioned above.

2 Editorial Office's comments

1) Science Editor: The authors presented 4 cases of MALS successfully managed by medical therapies. The subject is interesting, there are few reports in the literature describing more than one case. However, the manuscript needs a careful review of wording and phrasing by an expert on English language. Additional comments: -

Indicate the posology and duration of the treatments administrated. - The patients were treated with different drug protocols (amitriptyline, tegoprazan, gabapentine, meloxicam, famotidine, esomeprazole…). Please outline the reasons to choose one over another in each specific clinical scenario. - Indicate the alternative surgical treatments for MALS, together with their expected outcomes based on the literature. - Describe a proposed algorithm to diagnose MALS in patients in which the disease is suspected. State the different imaging alternatives, their typical findings, and state the gold standard exploration to reach a definitive diagnosis. - Have you planned any additional treatments for the patients not presenting a complete relief of the digestive symptoms? Please add images

Answer: Please see the answers to the peer reviewers' questions. Figures were added at the end of the text, before the figure legends.