

July 28, 2021

Dear reviewers,

Thank you for the opportunity to resubmit our manuscript entitled “Thoracoscopic resection of a large lower esophageal schwannoma: A case report and review of the literature”(manuscript No. 69007)). Below please find a detailed point-by-point reply to your comments. Changes in the manuscript can be found in track changes. In addition, We have invited native speakers to polish the manuscript.

1. The reason why lower esophageal schwannomas are rare is not mentioned in this manuscript. Furthermore, the characteristics of lower esophageal schwannomas are required in the discussion part.

Response: We feel great thanks for your professional review work on our article. The question you raised is very significant. Through reviewing the kinds of literature, we found that the reason why lower esophageal schwannomas are rare has not been clearly reported. Therefore, we have discussed it in the article. Anatomically, the innervation of the striated muscle in the pharynx and the upper esophagus originates from the brain stem, but the nerve of the distal esophagus originates from the dorsal motor nucleus of the vagus nerve and ends at the ganglion of the myenteric plexus^[1]. It has been shown that there are two peak areas of innervation in the cervical and thoracic regions of the esophagus in canines^[2]. We speculate that the incidence of esophageal schwannoma may be related to the origin and distribution of the nerve plexus; however, but no study has confirmed it clearly at present, which. This makes it is a significant study worthy of further exploration in the future. To our knowledge, we are the first to conduct a statistical analysis of the lower esophageal schwannoma, hoping to contribute to the clinical diagnosis and treatment. We have discussed the characteristics of clinical data, symptoms, diagnosis, and treatment on the lower esophageal schwannoma in the

discussion part.

2. In page 7, gender seems different in lower schwannoma compared with all schwannomas. It is hard to say this conclusion from the small number of the cases.

Response: Thanks for your careful check. It is really true as you suggested that it is hard to say this conclusion from the small number of the cases. In order to make the article more rigorous, we have deleted this conclusion.

3. The usefulness of Sox10 immunostaining is reported in soft-tissue neoplasia. Are there any studies assessed with esophageal schwannomas? Otherwise, the conclusion that Sox 10 is superior to S100 is not adequate in this esophageal schwannoma.

Response: Thank you for your reminder. To the best of our knowledge, we were the first to use Sox10 to detect esophageal schwannomas. According to your nice suggestion, We have revised the conclusion about Sox10 as “Studies revealed that Sox10 may be a potential molecular marker for esophageal schwannomas, but further studies with large samples for an in-depth investigation on Sox10 are required.”

4. A reviewer requests a literature review to compare lower esophageal schwannoma and upper/middle schwannoma. It may enable them a statistical analysis.

Response: Thank you for your nice suggestion on our article. your suggestion really means a lot to us. First of all, we have added a table (Table I) to analyze clinical data of the lower esophageal schwannomas and upper/middle esophageal schwannomas and found that there were fewer cases of the lower esophageal schwannomas (13) than upper/middle esophageal schwannomas (57), which is similar to previous reports. In addition, we conducted a literature review on clinical data, symptoms, differential diagnosis, and treatment to compare the lower esophageal schwannomas and upper/middle esophageal schwannomas in this paper. This will be helpful for the diagnosis and treatment of the lower esophageal schwannoma.

Thank you again for your consideration of this manuscript.

Yours sincerely,

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2. **Khurana RK**, Petras JM. Sensory innervation of the canine esophagus, stomach, and duodenum. *Am J Anat* 1991; **192**: 293-306 [PMID: 1759692 DOI: 10.1002/aja.1001920309]