February, 14, 2015

Dear Editor,

We are very grateful to you and to the reviewers for your helpful advices

Please find enclosed the edited manuscript in Word format (file name: 15876-review.doc).

Title: Solitary distant recurrence of gastrointestinal stromal tumors in the left brachialis muscle

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The manuscript has been improved according to the suggestions of reviewers:
1. Format has been updated.
2. Revision has been made according to the suggestions of the reviewer.

- Revisions

1) (1) There is no need to list all normal laboratory findings in detail, as they may not be useful for diagnosis of this disease.
   ➔ We have summarized the laboratory findings in the manuscript.

   (2) The authors stated that the mass in the left arm decreased in size after imatinib therapy, why didn't they consider surgical resection of the tumor for this patient?
   ➔ Thank you for your suggestions. At this time, she was considered for surgical resection of solitary metastatic muscle mass. However, she presented poor performance because was very old and had Parkinson's disease. She was diagnosed with high-risk GIST. High–risk GIST is associated with an increased recurrence and a decreased survival despite complete surgical resection (Hassan I et al., Ann Surg Oncol 2008;15(1):52-59). Therefore, she was administered imatinib instead of undergoing surgical mass resection. We added this information for the case and in the discussion.

   (3) The patient cannot tolerate the side effects of imatinib, why not choose second-line drugs?
   ➔ The patient refused further treatment as a result of the underlying disease and deterioration in her general condition. Thank you for providing an accurate comment in the respect.

   (4) In DISCUSSION Section, discussions about the four cases of GIST with metastasis to skeletal muscle reported previously are not enough. More on their treatment and prognosis should be discussed.
   ➔ We added more information for four cases of GIST with a metastasis to the skeletal muscle. Thank you for your detailed comments

   (5) Some references missed years. The format of references should be unified.
   ➔ We corrected the references.

(6) Please provide Figure 2 once again. It cannot be seen in the context
➔ We provided the relevant figure again.

2) (1) Actually, three of five (including current paper) cases with muscle metastasis are derived from GIST of the small intestine. Considering the occurrence frequency of primary GIST in the small intestine, the high proportion is outstanding. Please comment this fact and the plausible pathophysiology.
➔ Thank you for your comment. GIST occurred in the stomach in about 70% of the cases, in the small intestine in 20%, and in the esophagus less than 10%. Tumors of small-bowel origins tend to exhibit more aggressive behavior and thus result in a worse prognosis than for tumors originating in other gastrointestinal sites. In addition, an overtly malignant behavior is less commonly seen in gastric tumors (Dematteo RP et al, Cancer 2008;112:608–15). We added this information to the discussion.

(2) Authors well described the reported mechanisms of resistance against cancer cell invasion and metastasis in muscle. However, this case reversed the theory. Is there any possibility that any pathological alterations of muscle induced by the factors such as high aged and concomitant Parkinson's disease contributed the occurrence?
➔ Thank you for your excellent comment. We checked for an association between Parkinson's disease and a malignancy. Parkinson's disease indicated an increased risk for melanoma and breast cancer (Garber K, J Natl Cancer Inst. 2010;102(6):371-4). However, it does not appear to be related to a risk for a muscle malignancy and hematogenous muscle metastasis. We also searched broadly in the extant research with respect to a relationship between aging and hematogenous muscle metastasis. However, I am sorry to did not find any results.

3) (1) The references are not standardly written. Year is leaked in some papers (e.g. 6, 7, 16).
➔ We corrected references.

3 References and typesetting were corrected
➔ We added PubMed citation numbers and DOI citation of the reference list.

4. Figures were corrected that the fonts and lines can be edited or moved.
(For the figures, the fonts and lines can be edited or moved. It can be made by ppt.)
➔ We corrected for the fonts and the lines in the figures to be edited as a ppt file.

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

Best regards

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