Author's response to reviews

**Title:** The clinicopathological observation, c-kit gene mutation and clonal status of gastrointestinal stromal tumor in sacrum

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**Author's response to reviews:** see over
Dear editor and reviewers,

We are truly grateful to yours and other reviewers’ critical comments and thoughtful suggestions. Based on these comments and suggestions, we have made careful modifications on the original manuscript. All changes made to the text are in red color. In addition, we have consulted native English speakers for paper revision before the submission this time. We hope the new manuscript will meet your magazine’s standard. Below you will find our point-by-point responses to the reviewers’ comments/questions:

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To Reviewer: Giuliano Ramadori

1. I have provided a new CT photograph representing the lesion to involve sacrum.
2. The manuscript has been proofread by an English speaking professional with science background at Shinewrite Corporation.
3. I have added the reference (2-4 and 8-10).
4. I have looked up carefully the main reference (No.5) in PubMed, and found its publication year to be 2006 instead of 2005.
5. I have revised the numbering of the figures.

General comments:
The changes are marked in red.

Title: “…of a gastrointestinal stromal tumor in the sacrum (semicircular root of the fifth lumbar vertebra?)”
I will add “(semicircular root of the fifth lumbar vertebra)” in the title if you think it to be necessary after seeing the new CT photograph.

Abstract:
Page 1, line 1: “It is very rare that a…”
Yes, I have revised it.
Page 1, line 2: “…occurring in the…”
Yes, I have revised it.

Page 1, line 2: what is “intracal metabasis”? see also page 3, line 8.
Yes, I have revised it.

Page 1, line 3: “… reported in the literature… “…published in the literature”.
Yes, I have revised it.

Page 1, line 4: “… we present..”, instead of “presented”.
Yes, I have revised it.

Page 1, line 5: “…in the sacrum and elucidate its…”, instead of “in sacrum in order to elucidate the..”.
Yes, I have changed “in sacrum in order to elucidate the..” to “…in the sacrum and describe its….”

Page 1, line 9: “exons 9, 11, 13, and 17.”
Yes, I have revised it.

Page 1, line 10: “mosaics”?
Yes, I have changed “mosaics” to “mosaicism”.

Page 1, line 12: “were examined.”
Yes, I have revised it.

Page 1, line 12: “…the lesion”
Yes, I have revised it.

Page 1, line 13: “Trabecula…”
Yes, I have revised it.

Page 1, line 15: “staff-like”? 
Yes, I have deleted it.

Page 1, line 15: “Mitosis figures were rare.”
Yes, I have changed it to “Mitotic figures”.

Page 1, line 17: “a c-KIT…”
Yes, I have revised it.

Page 1, line 18: “that the GIST”
Yes, I have revised it.
Page 1, line 18: Delete: “GIST is a neoplastic lesion.” – known.
Yes, I have deleted it.

Page 1, line 19: “It is very rare that GISTs occur in the sacrum”, change to “In summary, we show that tumor material, phenotypically identical with GISTs was found in bone of the semicircular root of the fifth lumbar vertebra.”
Yes, I have revised it. But I have changed “…bone of the semicircular root of the fifth lumbar vertebra” to “sacrum”. Because the lesion is only found in the sacrum. I will change to “semicircular root of the fifth lumbar vertebra” if you think it to be necessary after seeing the new CT photograph.

Page 1, line 19: “It is difficult to differentiate GISTs from…”
Yes, I have revised it.

Page 1, line 20: “…hence the need for immunohistochemistry…”, instead of “so it should be diagnosed by…”
Yes, I have revised it.

Background:
Page 3, paragraph 1, line 2: “…they are supposed to arise from….”, instead of “that arise…”
Yes, I have revised it.

Page 3, paragraph 1, line 6: “and the retroperitoneal space”
Yes, I have revised it.

Page 3, paragraph 1, line 7: “…it is very rare that GISTs occur in the sacrum.”
Yes, I have revised it.

Page 3, paragraph 1, line 9: “…we present a rare case…occurring in the sacrum…”, instead of “presented”.
Yes, I have revised it.

Page 3, paragraph 1, line 10: “…We describe and discuss…”, instead of “described and discussed.”
Yes, I have changed it into “describing and discussing…”.
Page 3, paragraph 1, line 11: “…for the pathologist.”
Yes, I have revised it.

Page 3, paragraph 1, line 13: “…in the bone”.
Yes, I have revised it.

Page 3, paragraph 1, line 12: “to further confirm”.
Yes, I have revised it.

**Materials and Methods:**

Page 3, paragraph 2, line 2: “dyschesia?”
Yes, it is “dyschesia”

Page 3, paragraph 2, line 2: “...for three months...to the department...”
Yes, I have revised it.

Page 3, paragraph 2, line 4: “…swelling…”; “hemafecia”?; “crissum pain”? Yes, they are “…swelling…”, “hemafecia” and “crissum pain”.

Page 3, paragraph 2, line 5: “…pelvis…”
Yes, I have revised it.

**Methods:**

Page 4, paragraph 2, line 3: “…neuronal specific enolase…”
Yes, I have revised it.

Page 4, paragraph 3, line 3: “…dissected using…”, instead of “dissected out”. Yes, I have revised it.

Page 5, paragraph 2, line 4ff: replace “ml” for “mL” in the following paragraphs. Yes, I have revised it.

Page 5, paragraph 2, line 5: “…forward and reverse primers”, instead of “primers F and R”.
Yes, I have revised it.

Page 5, paragraph 2, line 11: “Then, direct sequencing was performed”, instead of “the direct sequencing were…”
Yes, I have revised it.

Page 5, paragraph 2, line 12: “…no mutation...except for exon 11.”
Yes, I have revised it.

Page 5, paragraph 2, line 15: “clones”
Yes, I have revised it.

Page 5, paragraph 2, line 16: “…of the digested…”
Yes, I have revised it.

Page 5, paragraph 2, line 17: “of the recombinant product.”
Yes, I have revised it.

Page 6, paragraph 1, line 1: “Nested PCR was used for amplification and detection of…”
Yes, I have revised it.

Page 6, paragraph 1, line 2+3: no abbreviation for “PGK” and “AR”
Yes, I have revised it.

Page 6, paragraph 1, line 3: Delete: “according to the following description”.
Yes, I have revised it.

Page 6, paragraph 1, line 8: “surrounding tissue”, instead of “non-lesions”.
Yes, I have revised it.

Page 6, paragraph 1, line 19: “…using the primers…”
Yes, I have revised it.

Page 7, paragraph 3, line 7: “or vice-versa”? the change of the denominator does matter.
Yes, I have revised it.

Page 7, paragraph 3, line 9: “mosaic”, instead of “mosaicism”.
It is “mosaicism” in most of the literatures, instead of “mosaic”. I will delete it if the reviewer think it to be wrong.

**Results:**

Page 8, paragraph 1, line 3: “Trabecula of bone were found…”
Yes, I have revised it.

Page 8, paragraph 1, line 7: “…desmin…”
Yes, I have revised it.

Page 8, paragraph 2, line 1: “of the c-KIT gene”
Yes, I have revised it.
Page 8, paragraph 2, line 4: “...confirmed further...”
Yes, I have revised it.
Page 8, paragraph 2, line 8: “...but not in the following domains...”
Yes, I have revised it.
Page 9, paragraph 1, line 3: “When the...”, delete “tissue”
Yes, I have revised it.
Page 9, paragraph 1, line 5: “...an obviously reduced...”
Yes, I have revised it.
Page 9, paragraph 1, line 6: “...suggesting...”, delete “and”.
Yes, I have revised it.

**Discussion:**
Page 10, paragraph 1, line 1: “Gastrointestinal stromal tumors (GISTs) are...”
Yes, I have revised it.
Page 10, paragraph 1, line 2: “...cases per million...”, delete “populations”.
Yes, I have revised it.
Page 10, paragraph 1, line 3: “The usual age at presentation...”
Yes, I have revised it.
Page 10, paragraph 2, line 1: “...mostly relies on...”
Yes, I have revised it.
Page 10, paragraph 2, line 3: “...was the positivity of the tumor cells for...”
Yes, I have revised it.
Page 10, paragraph 2, line 4: “...literature...”
Yes, I have revised it.
Page 10, paragraph 2, line 7: “schwannoma”
Yes, I have revised it.
Page 10, paragraph 2, line 8: “Based on histopathological...”, delete “detailed”.
Yes, I have revised it.
Page 10, paragraph 2, line 9f: “…immunohistochemical staining of..., the
results…characteristics.”
Yes, I have revised it.

Page 11, paragraph 1, line 1: “…the c-KIT gene…to further confirm the diagnosis…”
Yes, I have revised it.

Page 11, paragraph 1, line 2: “..but not in…”
Yes, I have revised it.

Page 11, paragraph 1, line 3: “Thus supporting the diagnosis of GIST in this case.”
Yes, I have revised it.

Page 11, paragraph 1, line 9: “electronic”?
Yes, It is “electronic”

Page 11, paragraph 1, line 10: “but no lesion was found.”
Yes, I have revised it.

Page 11, paragraph 1, line 11: “Can we explain….”
Yes, I have deleted it.

Page 11, paragraph 2, line 3: “…the peritoneum…”
Yes, I have revised it.

Page 11, paragraph 2, line 7: “previously…”
Yes, I have revised it.

**Figure legends**

Figure 2: “Trabecula”
Yes, I have revised it.

Figure 6A: “…a reduced intensity…”
Yes, I have revised it.

Figure 6B: “…an obviously reduced…”
Yes, I have revised it.

**Table 1**

“Length of PCR product”, instead of “magnitude…”
Yes, I have revised it.
“annealing temperature”
Yes, I have revised it.

Mutation analysis
Point out mutated region.
Yes, I have pointed out mutated region by arrow.

To Reviewer: Tadashi Terada

1. GIST may be converted into EGIST (extragastrointestinal stromal tumor)

Yes, but it was not clear whether the original lesion had disappeared or this GIST had occurred primarily in the bone. Moreover, the lesion was only found in the sacrum, but no other organs or position.

2. The sources of antibodies should be written.

Yes, I have written the sources of antibodies.

3. The relationship of testis should be written, because testicular germ cell tumors frequently show KIT gene mutation.

1) The patient is a woman;

2) Yes, I have added some contents related to germ cell tumors from female, such as dysgerminoma of the ovary, which is positive for CD117.

Best wishes!

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