Reviewer's report

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

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Reviewer: Giuliano Ramadori

Reviewer's report:

Comments to the Authors

In the recently submitted manuscript Li Gong, Yan-Hong Li, Hua-Dong Zhao, Jian-Ye Zhao, and Wei Zhang, entitled “The clinicopathological observation, c-kit gene mutation and clonal status of gastrointestinal stromal tumor in sacrum” the authors report on a case of a 50-year-old lady with a primary GIST of the sacrum.

Careful analysis to identify the tumor as GIST was done and included immunhistochemistry, mutation analysis and a clonal essay for the description of the tumor as monoclonal.

However there are several major problems regarding the manuscript. To our understanding, the CT-slice shown in figure 1 represents a section above the os sacrum, so that the tumor appears to rather involve the semicircular root of the fifth lumbar vertebra. The tumor should be pointed out in the image. The tumor appears faint and the question would be whether a computed tomography scan with contrast medium is available. If not, it would be possible that a primary tumor other than the tumor mentioned by the authors could have been missed at diagnosis.

Overall, the paper needs careful revision. To mention a few: Some references are missing (2-4 and 8-10), the main reference (No. 5) is cited with the wrong publication year (2005 instead of 2006), the numbering of the figures is not in accordance with the text, and the English needs major revision and editing.

At the present stage, the paper has to be rejected.

General comments:

The changes are marked in red.

Title: “…of a gastrointestinal stromal tumor in the sacrum (semicircular root of the
fifth lumbar vertebra?)”

Abstract:

Page 1, line 1: “It is very rare that a…”

Page 1, line 2: “…occurring in the…”

Page 1, line 2: what is “intracal metabasis”? , see also page 3, line 8.

Page 1, line 3: “… reported in the literature… “…published in the literature”.

Page 1, line 4: “… we present..”, instead of “presented”.

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

Page 1, line 9: “exons 9, 11, 13, and 17.”

Page 1, line 10: “mosaics”? 

Page 1, line 12: “were examined.”

Page 1, line 12: “…the lesion”

Page 1, line 13: “Trabecula…”

Page 1, line 15: “staff-like”? 

Page 1, line 15: “Mitosis figures were rare.”

Page 1, line 17: “a c-KIT…”

Page 1, line 18: “that the GIST”

Page 1, line 18: Delete: “GIST is a neoplastic lesion.” – known.

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.”

Page 1, line 19: “It is difficult to differentiate GISTs from…”
Page 1, line 20: “…hence the need for immunohistochemistry…”, instead of “so it should be diagnosed by…”

Background:

Page 3, paragraph 1, line 2: “…they are supposed to arise from…”, instead of “that arise…”

Page 3, paragraph 1, line 6: “and the retroperitoneal space”

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

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

Page 3, paragraph 1, line 10: “…We describe and discuss…”, instead of “described and discussed.”

Page 3, paragraph 1, line 11: “…for the pathologist.”

Page 3, paragraph 1, line 13: “…in the bone”.

Page 3, paragraph 1, line 12: “to further confirm”.

Materials and Methods:

Page 3, paragraph 2, line 2: “dyschesia?”

Page 3, paragraph 2, line 2: “…for three months…to the department…”

Page 3, paragraph 2, line 4: “…swelling…”; “hemafecia”?; “crissum pain”?

Page 3, paragraph 2, line 5: “…pelvis…”
Methods:

Page 4, paragraph 2, line 3: “…neuronal specific enolase…”

Page 4, paragraph 3, line 3: “…dissected using…”, instead of “dissected out”.

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

Page 5, paragraph 2, line 5: “…forward and reverse primers”, instead of “primers F and R”.

Page 5, paragraph 2, line 11: “Then, direct sequencing was performed”, instead of “the direct sequencing were…”

Page 5, paragraph 2, line 12: “…no mutation…except for exon 11.”

Page 5, paragraph 2, line 15: “clones”

Page 5, paragraph 2, line 16: “…of the digested…”

Page 5, paragraph 2, line 17: “of the recombinant product.”

Page 6, paragraph 1, line 1: “Nested PCR was used for amplification and detection of…”

Page 6, paragraph 1, line 2+3: no abbreviation for “PGK” and “AR”

Page 6, paragraph 1, line 3: Delete: “according to the following description”.

Page 6, paragraph 1, line 8: “surrounding tissue”, instead of “non-lesions”.

Page 6, paragraph 1, line 19: “…using the primers…”

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

Page 7, paragraph 3, line 9: “mosaic”, instead of “mosaicism”.
Results:

Page 8, paragraph 1, line 3: “Trabecula of bone were found…”

Page 8, paragraph 1, line 7: “…desmin…”

Page 8, paragraph 2, line 1: “of the c-KIT gene”

Page 8, paragraph 2, line 4: “…confirmed further…”

Page 8, paragraph 2, line 8: “…but not in the following domains…”

Page 9, paragraph 1, line 3: “When the…”, delete “tissue”

Page 9, paragraph 1, line 5: “…an obviously reduced…”

Page 9, paragraph 1, line 6: “…suggesting…”, delete “and”.

Discussion:

Page 10, paragraph 1, line 1: “Gastrointestinal stromal tumors (GISTs) are…”

Page 10, paragraph 1, line 2: “…cases per million…”, delete “populations”.

Page 10, paragraph 1, line 3: “The usual age at presentation…”

Page 10, paragraph 2, line 1: “…mostly relies on…”

Page 10, paragraph 2, line 3: “…was the positivity of the tumor cells for…”

Page 10, paragraph 2, line 4: “…literature…”

Page 10, paragraph 2, line 7: “schwannoma”

Page 10, paragraph 2, line 8: “Based on histopathological…”, delete “detailed”.

Page 10, paragraph 2, line 9f: “…immunhistochemical staining of…, the results…characteristics.”
the c-KIT gene...to further confirm the diagnosis...

but not in...

Thus supporting the diagnosis of GIST in this case.

electronic?

but no lesion was found.

Can we explain,...

...the peritoneum...

previously...

Figure legends

Trabecula

...a reduced intensity...

...an obviously reduced...

Table 1

"Length of PCR product", instead of "magnitude..."

"annealing temperature"

Mutation analysis

Point out mutated region.