Author's response to reviews

Title: A case of spontaneous regression of bone metastasis from renal cell carcinoma; Case Report

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Author's response to reviews: see over
Dear The BioMed Central Editorial Team,

Enclosed please find a revised manuscript by Takahiro Nakajima, et al #4495155486528136 entitled: “A case of spontaneous regression of bone metastasis from renal cell carcinoma: Case Report”. We made changes in the text thoroughly according to referee’s comments. Now we believe it suitable for publication for “BMC Cancer”. We are looking forward to your reply.

Reply for the comments from referees is enclosed on a separate page.

Thank you for your consideration in this matter.

Yours sincerely

Takahiro Nakajima, MD
To the Reviewer #1
Dear Dr. Christian Doehn,

We believe that the paper has been much improved, largely as a result of referee’s many thoughtful comments. I would like to explain below how we have responded to each comments.

(1). The authors must clearly state what happened after biopsy of the sternum. Why was there a delay of 2 months between biopsy (with histologic tumor) and operation (without histologic tumor). Was there another CT right before the operation?

We guess that there happened an inflammation after the biopsy of the sternum. An inflammation in the carcinoma tissue might cause an immunologic chain reaction and lead to the regression of the tumor. The reason of which we assume like that is as follows; the regressed tumor tissue was completely removed and carefully examined pathologically which revealed wide hemorrhagic area and infiltration of inflammatory cells especially for fibroblasts. We changed following sentences in the Case Report part.

“Pathological examination revealed only granulation tissue which composed of wide bleeding area and necrosis area with strong infiltration of inflammatory cells especially for fibroblasts.”

During the two month after the biopsy, we performed distant metastasis check up and check his physical function preparing for an operation. We took a chest CT prior to the operation after an admission, the tumor shadow was the same comparing with previous chest CT before the biopsy. We added following sentence in the Case Report part.

“We performed distant metastasis check up and check his physical function preparing for an operation. No evidence of other distant metastases was seen. We took a chest CT prior to the operation after an admission, the tumor shadow was the same comparing with previous chest CT before the biopsy.”
(2). Why was there no therapy for the sternal metastasis before operative removal?

We are sorry for miss typing of the date of appearance of disease and detected by CT. The patient diagnosed as metastatic renal cell carcinoma of sternum in September 2004 due to the CT guided percutaneous needle biopsy. There were no distant metastases except sternal bone metastasis, so we judged that we can perform complete resection of the tumor. Thus we didn't performed neither chemotherapy nor radiotherapy before the surgery.

(3). What is the rationale to treat this patients with adjuvant interferon? The given literature (Ljungberg et al.) is dealing with non-metastatic renal cell carcinoma!

We understand the reviewer's comment in this aspect. We added the two new reference papers as follows.


(4). Literature No.4 is not Jacob L but Lokich J.

We are sorry for mistake and changed as follows.

To the Reviewer #2

Dear Dr. Bruno Fuchos,

We believe that the paper has been much improved, largely as a result of referee’s many thoughtful comments. I would like to explain below how we have responded to each comments.

(1). *It is unclear why this patient was operated (for the metastasis) 14 months after biopsy.*

We are sorry for miss typing of the date of appearance of disease and detected by CT. The patient diagnosed as metastatic renal cell carcinoma of sternum in September 2004 due to the CT guided percutaneous needle biopsy and the operation was performed in November 2004. During the period, the patient received distant metastasis check up and checking for physical condition preparing for an operation.

(2). *More importantly, the authors mentioned that the resection was PARTIAL. This implies that there was no complete histological assessment of the entire tumor. Therefore, full evidence of complete spontaneous regression (as mentioned on page 4) is lacking.*

We performed the partial resection of the sternal bone with wide margin including whole tumor tissue and we checked the excision edge was negative for tumor tissue. We changed the sentence below in the Case Report part.

“*The patient underwent a partial resection of the sternal bone with wide margin including whole tumor tissue in November 2004.*”

(3). *Above all, the follow up of three months is therefore too limited.*

We continue the follow up until now and the patient can keep good condition without recurrence of the tumor. We changed the sentence below in the Case Report part.

“*He is now receiving interferon therapy and is in good condition without recurrence for eight months after surgery.*”
(4). In the discussion, the authors mentioned that the phenomenon of regression may have been induced subsequent to the biopsy. This is too speculative (coincidence), and there is no evidence at all.

We understand the reviewer's comment in this aspect. However, unfortunately the mechanism of spontaneous regression of renal cell carcinoma is still unclear. The resected specimen was carefully examined pathologically which revealed wide hemorrhagic area and infiltration of inflammatory cells especially for fibroblasts. Therefore we guess that there happened an inflammation after the biopsy of the sternum. An inflammation in the carcinoma tissue might cause an immunologic chain reaction and lead to the regression of the tumor. It seems too speculative so we changed the sentence as follows.

“One of the possible explanations of this phenomenon may in this case have been induced by the needle biopsy performed in order to diagnose the metastasis; or bleeding caused by the biopsy may have triggered a chain reaction of host immune responses.”