Author's response to reviews

Title: Intraarticular Hemorrhage Due To Bevacizumab In A Patient With Metastatic Colorectal Cancer: Case Presentation

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Author's response to reviews: see over
REVISION 1:

Revisions of the manuscript are made as follows:

Comments to authors:

1) Although the capecitabine plus bevacizumab regimen could be a treatment option (ASCO meeting abstracts 2008; 26s: abstr 15120), the standard therapy for metastatic colorectal cancer is a regimen containing oxaliplatin or irinotecan. The authors should describe why they administered capecitabine plus bevacizumab to the patient.

   REVISED-1) **Oxaliplatin or irinotecan-based chemotherapy cold not granted due to poor performance score.**

2) Please add information on inflammation and anemia.

   REVISED -2) Laboratory studies revealed a hemoglobin value of 10.2 g/dl; white blood count of 7800 /mm$^3$ (NR<10800), C-reactive protein 0.45 mg/dl (NR <0.4 mg/dl).

3) Information on radiation dose, fraction, and treatment efficacy or outcome could be useful for clinicians. Please provide more detailed information in this regard.

   REVISED -3) **palliative radiotherapy (3000 cGy in 10 fractions)** to the left knee region was administered to relieve the symptoms.

Minor comments

1) Line 10 of the CASE REPORT: Please explain the meaning of the phrase “After the first cure.” Do you mean “After the first course of the regimen”?

   REVISED-1) After the **first cure of the regimen** he presented with monoarthritis on the left knee.

2) Line 4 and 9 of the CASE REPORT: The word “capecitabine” is misspelled.

   REVISED-2) **capecitabine**

3) Line 26 of the DISCUSSION: Is the word “(life) treating (hemorrhage)” a misspelling of life-threatening?

   REVISED-3) …. cannot explain the **life-threatening** hemorrhage ….
REVISION 2:

Thank you for your interesting.

Revisions of the manuscript are made as follows:

Comments to authors:
Changes made as indicated by the reviewer (blue colour).
It is cross of minor mistakes (red colour).

ABSTRACT
Introduction: ….. It has some specific side effects including severe bleeding, wound healing problems, gastrointestinal perforation, proteinuria and hypertension.

Case report: We present a 65-year old Asian male patient with synovial metastasis of the knee who experienced intraarticular hemorrhage after bevacizumab treatment. He was presented with monoarthritis on the left knee.

KEY WORDS:
Bevacizumab, Colorectal cancer, synovial metastasis, intraarticular hemorrhage

INTRODUCTION
…. Survival rates has been increased from %41 to %66 between 1950 and 2000.

…. Later, targeted therapies beginning with bevacizumab in 2004 had improved the overall survival of metastatic colorectal cancer up to 2 years.

… It has some specific side effects including severe bleeding, wound healing problems, gastrointestinal perforation, proteinuria and hypertension.

… We report a case of knee joint metastasis colon adenocarcinoma who experienced intraarticular hemorrhage subsequent to bevacizumab treatment.

CASE REPORT
A 65-year old Asian man was diagnosed as stage 3 colon cancer and treated with adjuvant fluorouracil and leucoverin.

…Chemotherapy with capecitabine and bevacizumab was started (Capecitabine 1000 mg/ m² twice a day 1-14 days. Bevacizumab 7.5 mg/kg on the 1st day, every 21 days). Oxaliplatin or irinotecanbased chemotherapy could not be granted due to poor performance score-poor ECOG performance score.

…Bevacizumab and capecitabine at the same dose and frequency was restarted. After the first cure course of the regimen he presented with monoarthritis on the left knee.

… Laboratory studies revealed a hemoglobin value of 10.2 g/dl; white blood count of 7800 /mm3 (NR<10800), C-reactive and C-reactive protein 0.45 mg/dl (NR <0.4 mg/dl).
Laboratory studies revealed a hemoglobin value of 10.2 g/dl; white blood count of 7800 /mm3 (NR<10800), C-reactive protein 0.45 mg/dl (NR <0.4 mg/dl).
The MRI magnetic resonance imaging revealed synovial metastasis of the knee (Fig 1). Cytologic examination was not done, and he denied refused to have an arthroscopic biopsy.

DISCUSSION
…If these measures fail and joint instability cause significant pain external or internal fixation may be considerable considered.

CONCLUSION
…Clinicians should examine the symptoms of monoarthritis carefully in patients with treated with bevacizumab and should not continue the therapy until they rule out intraarticular hemorrhage.

Authors' contributions
…MU and HSC designed the work; MU wrote the paper, MU, HSC, SSG, BS, MO and HB followed up the patient.