Author's response to reviews

Title: Extra-skeletal multiple myeloma presenting with an atrial mass: a case report and a review of the literature

Authors:

Federica Vigo (federica.vigo@tiscali.it)
Patrizia Ciammella (patrizia.ciammella@asmn.re.it)
Riccardo Valli (riccardo.valli@asmn.re.it)
Elisabetta Cagni (elisabetta.cagni@asmn.re.it)
Cinzia Iotti (cinzia.iotti@asmn.re.it)

Version: 4 Date: 25 May 2012

Author's response to reviews: see over
To the Editorial Board of Journal of Medical Case Reports

Dear Sir,

we submit to Journal of Medical Case Reports: 
"Extra-skeletal multiple myeloma presenting with an atrial mass: case report and review of literature".

This case report may be added to literature as describes an unusual presentation of the disease and a new therapeutic approach to this manifestation of multiple myeloma.

The authors declare that they have no competing interests.

I’m at your complete disposal for any additional explanation or integration.

Thanks of all.

My best Regards,
Federica Vigo

Department of Advanced Technologies, Radiation Oncology Unit, Arcispedale Santa Maria Nuova - IRCCS Reggio Emilia, Italy.
Tel.: ++39 3470664567
Fax: ++39 0522 296392
e-mail: federica.vigo@tiscali.it
Dear reviewer,

we worked diligently to revise our manuscript entitled "Extra-skeletal multiple myeloma presenting with an atrial mass: a case report and a review of the literature" in response to the thorough and insightful reviews. We greatly appreciate your time and effort in assisting us with making our manuscript a stronger scientific contribution. The revised document has been submitted electronically as is the usual practice. The following text reflects our revisions.

SPECIFIC COMMENTS

1) This case report refers on a rare extra-medullary localization of Multiple Myeloma (heart). Few cases are reported in medical literature, most of them treated with systemic therapies. The case describes a treatment approach with radiation therapy (rarely employed and of interest).

Authors reply: Thank you very much for you positive comment.

2) More details should be provided on disease presentation at diagnosis (disease sites) and on 1st and subsequent systemic therapies, as well as response.

Authors reply: We added this information in the text

A healthy 79-year-old caucasian woman was referred to our hospital with a diagnosis of stage III immunoglobulin A-lambda multiple myeloma (MM) with numerous osteolytic areas (bilateral iliac wings, T3-T4) and cardiological symptoms of pulmonary embolism

3) When cardiac relapse was diagnosed the patients was re-staged? No data are provided on global disease presentation.

Authors reply: the patient, when cardiac relapse was diagnosed, was restaged.

We added this information in the text:

Restaging examinations documented stable bone disease

4) A detailed report on pre- and post-RT cardiological evaluations (ecocardiographic findings, functional data, medical therapy prescribed by cardiologist) should be provided.

Authors reply: We added this information in the text:

Transesophageal echocardiogram revealed a large pericardial effusion with evidence of cardiac tamponade and a large right atrial mass encasing the interatrial septum extending into the left atrium.

A transesophageal echocardiogram performed after three weeks from the end of RT confirmed a significant decrease in tumor size in the right atrium.

5) Technical details on RT should be given, as they could be very useful (immobilization devices, margins, planning, dose constraints)

Authors reply: We added this useful details

The patient was immobilized in the supine position with a Wing Board Device and target localization was accomplished using CT simulation. The volumes of interest were identified on each axial CT slice. Gross tumor volume (GTV) was defined as the gross extent of the tumor shown by imaging (CT, MRI and PET); clinical target volume (CTV) was defined as the GTV plus a margin for potential microscopic spread (5 mm), while, in order to account for organ motion and patient setup errors, the planning target volume (PTV) was defined by adding a 1-cm margin to CTV. Treatment planning was performed using an inverse planning algorithm in
Tomotherapy planning system and the patient was treated with an intensity modulated radiation therapy (IMRT) delivered with Tomotherapy.

6) Response evaluation: only a CT scan on June 2010, and then nothing until 2011 when maintenance therapy was started: why? are there other CT, MRI or ecocardiographic findings available? why starting maintenance after 8 months?

Authors reply: the patient was submitted to a new chest and abdominal CT on December 2010, that showed a bony PD, but maintenance therapy was started after 8 months from the end of radiation therapy because of a worsening of general conditions.

We added this information in the text:

Due to the patient’s age and good conditions, the medical staff chose a “wait and see” approach. Three months later a new chest and abdominal CT showed cardiac CR (complete remission) but a bone PD (progression disease).

The worsening of the general conditions of the patient, due to other causes, meant that she was subjected to supportive care for two months; following the improvement of health status, the patient started maintenance chemotherapy with Lenalidomide and she is currently tolerating it well.

7) No data are provided on the clinical course of MM after RT (good conditions and no symptoms: what does it mean? how is evolving MM?)

Authors reply: this data was added:

Currently, the patient is generally in good condition and shows no significant cardiac symptoms. She has recently performed a chest and abdominal CT that has documented stability of disease in known locations but highlighted the emergence of an axillary mass, for which we are programming a new radiation treatment, in view of good response to previous radiotherapy.

8) A comment should be provided on the impact of RT: only symptomatic or we can consider a beneficial effect in delaying disease progression?

Authors reply: our comment on the impact of RT is the following:

In this case, the radiation treatment was useful not only to reduce the bone pain, but also to decrease cardiac disease burden with an immediate improvement in patient’s symptoms and performance status.

This result leads us to suggest the possibility to obtain not only a control of the symptoms, but also a beneficial effect in delaying disease progression.

9) Literature review: table 1 is not clear, probably table 2 is sufficient to present data on cardiac localizations, but in the text no comments are given (discussion) on the comparison between systemic treatments alone or local treatments + systemic therapies. Are the response comparable (chemotherapy and/or local therapies)? Are response comparable between surgery and RT? (RT seems safer than surgery, as the complication rate seems lower)

Authors reply: We acknowledge the reviewer comment; we simplified the table on review of the literature and made the following comment in the discussion section:

If we analyze the studies reported in Tab. I, it is quite evident how the radiation therapy, in cases in which it was administered, especially when associated with systemic therapy, has resulted, for a clinical and instrumental response, better than the other treatments, especially considering the better toxicity profile of radiation therapy compared with surgery. Another
possible alternative would seem to be the intrapericardial injection of different drugs, that, in the few cases reported in literature \(^5^,^6^,^8\), seem to have allowed a reasonable local control

10) This case report describes an interesting rare cardiac presentation of multiple myeloma in an elderly patient suggesting radiotherapy as a feasible and well-tolerated option for the treatment of heart involvement.

**Authors reply:** Thank you very much for your positive comment.

11) The size of atrial mass at diagnosis has not been reported. Were there cardiological symptoms at diagnosis (January 2009)?

**Authors reply: this data was added:**
A healthy 79-year-old caucasian woman was referred to our hospital with a diagnosis of stage III immunoglobulin A-lambda multiple myeloma (MM) with numerous osteolytic areas (bilateral iliac wings, T3-T4) and cardiological symptoms of pulmonary embolism. A chest CT documented the presence of a right atrial mass (42 x 53 mm), confirmed by subsequent MRI and F18-FDG PET. Transesophageal echocardiogram revealed a large pericardial effusion with evidence of cardiac tamponade and a large right atrial mass encasing the interatrial septum extending into the left atrium.

12) Before radiotherapy the patient was treated with chemotherapy (VMP regimen) but the response to this treatment, particularly the efficacy (or not) on atrial localization has not been reported. How many cycles of chemo were administered?

**Authors reply: data had been modified in this way:**
The patient was treated with 4 cycles of bortezomib, 4 cycles of MP (melphalan and prednisone) and another 4 cycles of bortezomib, achieving a lessening of the symptoms and a stability of cardiac disease.

13) "Case presentation" - third paragraph: VMP (bortezomib, melphalan and prednisone) is not a combination of different regimens. It is, by itself, a regimen called VMP based on the combination of three different drugs. The sentence could be changed in: "She was treated with xxx cycles of VMP (bortezomib, melphalan, prednisone) achieving...."

**Authors reply: data had been modified in this way:**
The patient was treated with 4 cycles of bortezomib, 4 cycles of MP (melphalan and prednisone) and another 4 cycles of bortezomib, achieving a lessening of the symptoms and a stability of cardiac disease.

14) Describe the size of the mass at the end of the radiotherapy (CT scan of June 2010)

**Authors reply: This data was added:**
A transesophageal echocardiogram performed after three weeks from the end of RT confirmed a significant decrease in tumor size in the right atrium. Three months later a new chest and abdominal CT showed cardiac CR (complete remission) but a bone PD (progression disease).

15) Needs some language corrections before being published

**Authors reply:** We have now partly rephrased the paper. We hope to have complied with the timely reviewer suggestion.
16) I had a positive opinion of the manuscript. Though some other similar works are reported in literature, the authors describe a very interesting situation due to peculiar remarks and unusual vessels aggressiveness of the disease. Even the specified therapeutic aspects are worth considering.

Authors reply: Thank you very much for your positive comment.