Denosumab treatment for Giant Cell Tumors of the Bone: Response evaluation and radiological patterns

Poster No.: C-2372
Congress: ECR 2017
Type: Scientific Exhibit
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Keywords: Musculoskeletal soft tissue, Oncology, CT, Ultrasound, MR, Image compression, Education, Multidisciplinary cancer care
DOI: 10.1594/ecr2017/C-2372

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Aims and objectives

To evaluate imaging assessment of response to treatment with Denosumabin cases of giant-cell tumors of bone (GCTB).
Methods and materials

We retrospectively reviewed 41 cases of biopsy-proven cases of GCTB in the period 1995-2015. Five of these 41 cases were treated with Denosumab. There were 2 men and 3 women, with an average age of 34 years. The indications for Denosumab treatment were: 3 unresectable and 2 recurrent lesions. Follow-up and response evaluation were performed with CT exclusively in 2 cases, with both MRI and CT in 2 cases, and with ultrasonography and MRI in 1 case. The most characteristic imaging findings were recorded. RECIST and Choi criteria were used for response evaluation.
Results

INTRODUCTION

Giant-cell tumors of the bone (GCTOB) is a lithic tumor of locally aggressive behavior that affects young patients and is prone to be found in the epiphyses-metaphyses region of the long bones, although other less frequent locations are the spine and pelvis.

The conventional treatment is surgical. However, the choice of surgical technique is a controversial matter, as it is prone to be found close to joints, young patients, and due to the high rate of locoregional recurrence.

In recent years, the introduction of denosumab has enabled the development of new therapeutic possibilities for the treatment of GCTOB. It is a monoclonal antibody with high affinity to the RANK-Ligand (which is responsible for the formation and activation of osteoclasts) producing an inhibition of bone destruction, elimination of giant cells, and promoting the formation of differentiated bone tissue Fig. 1 on page 8

Nowadays, its use is accepted in unresectable GCTOB (in locations of difficult surgical approach or with high patient morbidity rates) and/or recurrent.

RESULTS:

The treatment with denosumab causes both micro and macroscopic changes, which are not described in depth in the literature due to its recent therapeutic application in GCTOB.

Histologically, it is characterized by the disappearance of the giant cells with the formation of osteoid matrix and trabecular bone Fig. 2 on page 8

To define the radiological findings and to be able to establish a response to the treatment, we have followed up 5 patients who were diagnosed with GCTOB and who were treated with denosumab:

CASE 1
A 51-year-old woman diagnosed in 2009 with GCT on the distal radius Fig. 3 on page 9, who required multiple surgical interventions for local recurrence Fig. 4 on page 10. The last surgery was performed in 2012 with a vascularized fibular graft with instrumented arthrodesis between the graft and carpal. In spite of all the interventions performed, a new recurrence at the volar level of the wrist was diagnosed Fig. 5 on page 11. In tumors committee, it was decided to start treatment with denosumab.

*Radiological follow-up:* Due to its superficial location, it was decided to perform follow-ups through ultrasound. The follow up showed a decrease in size, appearance of intralesional calcifications, and disappearance of the Doppler signal, which was observed in the basal study Fig. 6 on page 12.

**CASE 2**

A 35-year-old patient with sacral GCTOB, initially oriented as sarcoma of gynecological area with bone invasion. Fig. 7 on page 13. In tumor committee the unresectability of the tumor was agreed, thus being a candidate for treatment with denosumab.

*Radiological follow-up:* It was controlled with CT and showed a reduction in size and in density Fig. 8 on page 14, as well as an increase in bone remodeling. Fig. 9 on page 15.

**CASE 3**

A 24-year-old male with unresectable sacral GCTOB Fig. 10 on page 16, starting treatment with denosumab. No other antecedents of interest.

*Radiological follow-up:* Through CT a clear decrease in tumor density was observed Fig. 11 on page 17, as well as bone remodeling. No conclusions were reached regarding changes in its size.

**CASE 4**

A 23-year-old woman with GCT in the left sacroiliac region Fig. 13 on page 19. Fig. 14 on page 20 who was surgically treated. One year later, she went through surgery again due to sacral recurrence through curettage and cementation of the cavity Fig. 15 on page 21. The part of the injury located in S2 could only be treated with curettage, due to cortical destruction of the left superior wall of the left anterior saccular foramen S2-S3, being considered as a "non-oncologic" surgery. Given the high probability of local persistence/recurrence, it was decided to start treatment with denosumab.
Radiological follow-up: Controls were performed using CT and no signs of local recurrence were identified. At the bone level, a greater bone remodeling was observed, as well as a consolidation of a small fracture due to insufficiency from post-surgical changes Fig. 16 on page 22.

CASE 5

A 48-year-old male with unresectable GCTOB diagnose at the sacrum level Fig. 17 on page 23. Joint treatment with radiotherapy and denosumab was started in October 2013. There were irregularities in the therapeutic adherence between May and November 2014.

Radiological follow-up: Mainly performed through CT. A clear reduction in size and in density was identified Fig. 18 on page 24 as well as an increase in bone remodeling Fig. 20 on page 25. Control through MR shows a clear reduction in T2 sequences, nonetheless these findings are not conclusive as he had previously received radiotherapy.

In the control TC performed after the period of therapeutic abstinence, some focus enhancement (190HU) compatible with an area of tumor viability were identified. After treatment resumed, no pathological enhancements were observed in subsequent controls Fig. 19 on page 26.

DATA ANALYSIS

Given that Case 4 did not have recurrence of GCTOB, it will be excluded both in the radiological findings and in the analysis of the response to treatment.

The most frequent radiological findings were:

- Bone remodeling - intralesional calcifications: 100% (4/4 cases)
- Density reduction: 100% (3/3 cases)
- Mild-moderate reduction in size: 75% (3/4 cases)
- As isolated data, it is worth noting the absence of Power Doppler signal in the ultrasound study (1 case) and the decrease in intensity of T2 sequences (1 case)

TREATMENT RESPONSE
• We analysed treatment response through RECIST and CHOI criteria. 75% of cases studied through TC and ultrasound had a partial response according to RECIST criteria (3/4 cases).

• 100% of the cases studied through TC had a partial response according to CHOI criteria (3/3 cases).
Fig. 1

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Fig. 2

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Fig. 3

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Case 1: First recurrence

Fig. 4

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Case 1: Second recurrence

Fig. 5

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Case 1: Ultrasound imaging

Fig. 6

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Case 2

Fig. 7

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Case 2: Pattern of contrast enhancement

Fig. 8

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Case 2: Bone formation and re-cortication

Fig. 9

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Fig. 10

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Case 3: Pattern of contrast enhancement

Fig. 11
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Case 3: Bone formation and re-cortication

![Images showing pre-treatment, 5 months, and 12 months scans]

**Fig. 12**

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Fig. 13

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Fig. 14

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Case 4: Recurrence

Fig. 15

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Case 4: Bone formation and re-cortication

Fig. 16

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Fig. 17

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Case 5: Pattern of contrast enhancement

Fig. 18

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Case 5: Bone formation and re-cortication

Fig. 20

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Case 5: Area of tumor viability

Fig. 19

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Conclusion

It is important to recognise the different patterns of radiological response to treatment with denosumab, as it may be the only therapeutic alternative in unresectable or recurring GCTOB.

In our experience the most frequent findings were increased bone remodeling-intralesional calcifications (100%), decrease in density (100%) and decrease in size (75%).

The decrease in the T2 signal is difficult to assess, as it was only found in one case, which also had received RDT with curative intent.

For the evaluation of the response to treatment, it is recommended to use the CHOI criteria if the follow-up is done through TC-MD, and the RECIST criteria for ultrasound or RM follow-up.
Personal information


References

-Radiological and pathological characteristics of giant cell tumor of bone treated with denosumab
Michiyuki Hakozaki, Takahiro Tajino, Hitoshi Yamada, Osamu Hasegawa, Kazuhiro Tasaki, Kazuo Watanabe and Shinichi Konno

-Objective tumor response to denosumab in patients with giant cell tumor of bone: a multicenter phase II trial

-Giant-cell tumor of bone, anti-RANKL therapy
Armelle Dufresne, Olfa Derbel 2, Philippe Cassier, Gualter Vaz, Anne-Valérie Decouvelaere and Jean-Yves Blay

-Giant-cell tumor of bone: treatment options and role of denosumab
Arun S Singh, Neal S Chawla, Sant P Chawla

-The Clinical Approach Toward Giant Cell Tumor of Bone
Lizz Van Der Heijden, P.D. Sander Dijkstra, Michiel A.J. Van De Sande, Judith R. Kroep, Remi A. Nout, Carla S.P. Van Rijswijk, Judith V.M.G. Bov´Ee, Pancras C.W. Hogendoorn, Hans Gelderblom