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Is Denosumab Boon Or Bane In Complicated Giant Cell Tumour Treatment? - Single Institution Experience - 72 Cases

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BACKGROUND

Giant Cell tumours (GCT) though benign give an orthopaedic oncosurgeon a tough time when its complicated. Recurrent, fungating, heavily pre-treated, pelvic and spine GCTs are very difficult to treat primarily by surgery. The invention of the drug, Denosumab, RANKL inhibitor has changed the scenario of management. The adjuvant use of it has made many young productive adult population back to their work which was nearly impossible few years back. Not much of an answer is there about when to stop the drug, rate of recurrence after Denosumab therapy, difficulties for a surgeon after therapy and the side effects encountered. We present to you our experience of Denosumab usage at our institution in seventy two patients.

INTRODUCTION & AIMS

Giant cell tumours are known to express RANKL (receptor activator of nuclear factor κ B ligand) and are responsible for the aggressive osteolytic nature of the tumour. Denosumab is a fully human monoclonal rankl antibody (IgG2) that targets and binds with high affinity and specificity to RANKL, thus inhibiting osteoclast differentiation, activation, and survival. In this longitudinal study we present our interim experience with denosumab in patients with giant cell tumors.

METHODS

Among a cohort of Seventy patients with giant cell tumors, thirty five patients who completed a median followup of one year from date of completion of treatment were analysed for pathological response [Fig 1], radiological response using PET CT scan [Fig 2], clinical response using Musculoskeletal Tumor Scoring Society questionnaire. Data were analysed using paired t tests and Kaplan Meir Survival analysis.

Results: Results: 51.4% of patients had local disease , 40% recurrent disease and 5.7% locoregional disease and 2.9% with metastases at presentation. 88.5% of patients had completed CT with denosumab with

at least a mean of 6 cycles. There was good pathologic response in 91.4% of patients and best overall clinical response was seen in 79.2% after completion of treatment as per the new classification devised in HCG . There was a significant improvement in estimated mean DFS with 30.4 months in denosumab arm compared to 12 months in others (Log rank Mantel Cox= 5, p=0.03) . The recurrence rates following denosumab treatment was only 3.4%. There was a significant improvement in quality of life scores on MSTS (emotional, pain, walking, gait, support) during every followup visit compared to baseline (all p's<0.05) with improvement seen over followup period in both recurrent and new cases . Intraoperative difficult curettages, chances of incomplete curettage and side effects were analysed.

CONCLUSIONS

Denosumab is indeed a 'silver bullet' in the treatment of complicated Giant cell tumours. The drug can be used as a neo- adjuvant modality to achieve maximum functional and biologic results. The difficulties encountered in the treatment are mainly difficult curettage during surgery in all cases, chances of incomplete curettage and Avascular necrosis of both femora in a single case. Its better to give a single or two doses of denosumab as adjuvant therapy than giving a full injections as described before. Pelvis and large tumours may require more doses at discretion of the MDT tumour board. Also once the long term safety profile study is established it can even thought to be used as a single modality.

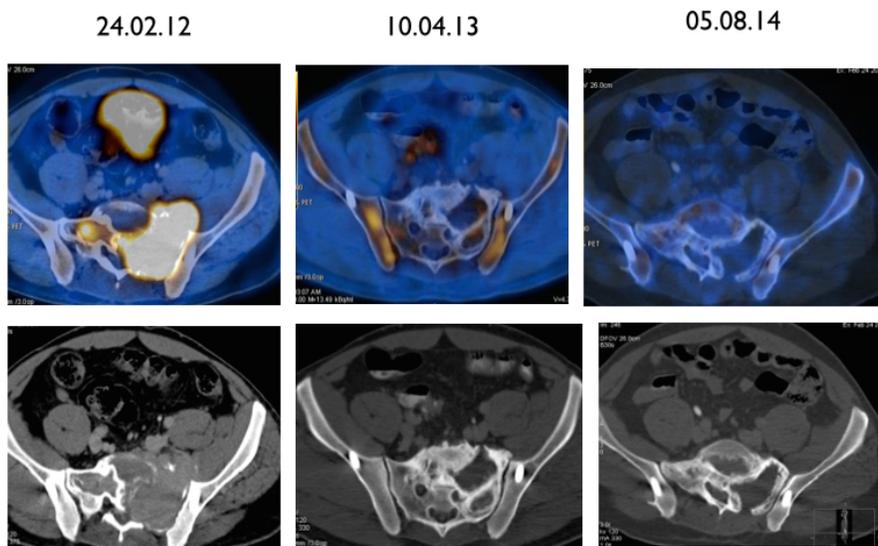
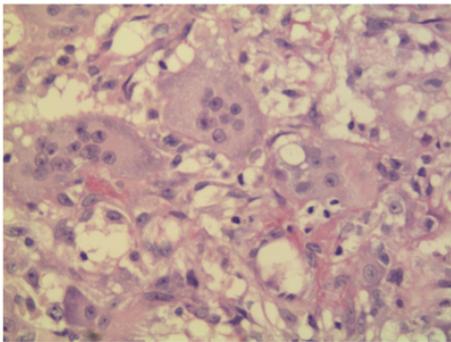


Figure 1.

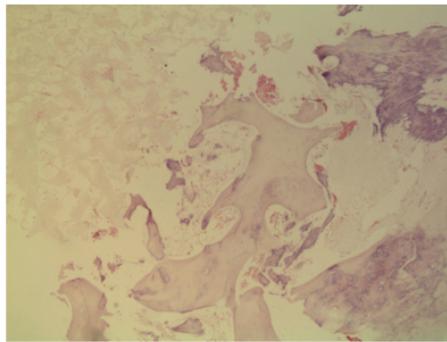
PET CT response of Recurrent Giant cell tumour of sacrum treated by Denosumab and embolisation

Figure 2.

PRETREATMENT MICROSCOPY



POST TREATMENT MICROSCOPY



Pathologic complete response showing no giant cells.