



GIANT CELL TUMOUR OF DISTAL RADIUS MANAGED BY PRE-OP DENOSUMAB THERAPY FOLLOWED BY EXCISION AND ULNAR TRANSLOCATION WITH WRIST ARTHRODESIS.

Orthopaedics

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ABSTRACT

Giant cell tumour of bone (GCTB) is a benign but locally aggressive neoplasm, accounting for approximately 5% of all the primary bone tumours. Denosumab is a human monoclonal antibody that inhibits RANK– RANKL binding thereby decreasing the formation, activity and survival of osteoclastic giant cells, resulting in reduced bone resorption. In some cases, in which tumour has broken through the cortex (grade 3) the distal end radius resected and reconstructed. Seradge described a novel technique of distal radius reconstruction by ulnar translocation with wrist arthrodesis. **Case report** Here is a case of 28 years old female with left distal radius GCT managed by neoadjuvant Denosumab therapy followed by complete excision with wrist arthrodesis and ulnar translocation. **Conclusion** Pre-op denosumab therapy makes subsequent surgery more feasible by surgical down-staging of the tumour and formation of hardened osteosclerotic rim around the tumour which helps in complete excision with no surgical spillage. Ulnar translocation is an easy, inexpensive method of reconstructing the distal end of the radius after excision.

KEYWORDS

GCT, Denosumab, ulnar translocation, wrist arthrodesis.

INTRODUCTION

Giant cell tumour of bone (GCTB) is a benign but locally aggressive neoplasm, accounting for approximately 5% of all the primary bone tumours^[1-3]. It commonly develops in the mature skeleton involving the epiphyseal region of long bones. In GCT, there is proliferation of mononuclear stromal cells which highly express Receptor activator of nuclear factor kappa-B ligand (RANKL) and an infiltrate of mononuclear macrophage-like cells and scattered multinucleated osteoclastic giant cells, both of which express RANK^[1,2,4,5]. Denosumab is a human monoclonal antibody that targets and binds specifically to RANKL; it competitively inhibits RANK– RANKL binding thereby decreasing the formation, activity and survival of osteoclastic giant cells in giant cell tumour, resulting in reduced bone resorption^[5-8]. The use of denosumab may convert an inoperable tumour to a resectable one by shrinking the extra-osseous component and ossifying tumour and therefore eventually improving the functional outcome^[9-11]. Previous studies have shown that pre-operative denosumab therapy makes the surgery more feasible and may result in surgical down-staging of the tumour,^[12, 13] allowing for improved patient function. Extended intralesional curettage followed by PMMA cement, bone substitutes or bone grafting remains the standard treatment solution for locally advanced or recurrent GCTB. The local extent of the tumour or anatomical constraints can sometimes disqualify a patient from this type of therapy. Uncurettable cases of GCTB when salvage of the joint is not achievable usually qualify for a segmental resection followed by reconstruction with a modular or patient-specific implant, biologic reconstruction with a bone graft or, in rare cases, amputation of the limb when local conditions, the advancement of the tumour or malignant transformation exclude limb-sparing surgery.^[14] In some cases, in which the tumour has broken through the cortex (Campanacci grade 3)^[15], with rapid growth, or when there is local recurrence, the distal end radius has to be excised and reconstructed.^[16-20]

The tumour removal and reconstruction of defect in GCT of distal radius is relatively difficult due to epiphyseal–metaphyseal location and presence of radial artery and median nerve in close proximity^[21]. The treatment modality for GCT of the distal end of the radius should suit patient best as per the profession and requirements. Various methods described include wide resection and reconstruction using structural autografts fibula (vascularized/non-vascularized), allograft, or centralization of the ulna with wrist arthrodesis and are reported with lower recurrence rate^[22-23]. Seradge described a novel technique of distal radius reconstruction by ulnar translocation along with its soft tissues^[24]. It has an added advantage of having a local vascularised graft without the need of microsurgical procedures but can lead to weaker grip strength and loss of movements at the wrist^[25]. Our aim was to evaluate the results of Campanacci grade-3 distal radius GCT treated pre-operatively with denosumab followed by En bloc excision of the tumour and ipsilateral ulnar translocation and arthrodesis of the wrist.

CASE PRESENTATION

Here is 28 years old female patient present with complains of swelling over left wrist since 6 months and pain over the swelling since 10 days. On examinations, swelling was bony hard in consistency with mild tenderness, well demarcated proximally, irregular in shape, fixed to the bone, non-reducible, non-fluctuant, non-compressible with normal overlying skin and engorged veins over it with no local rise of temperature. There was no distal neurovascular deficit and hand functions were normal.

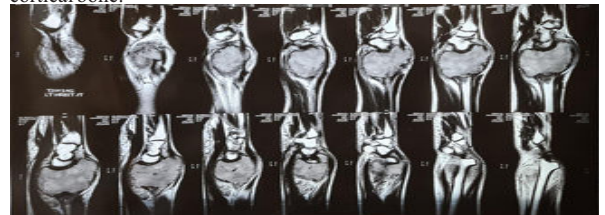
MATERIALS AND METHODS

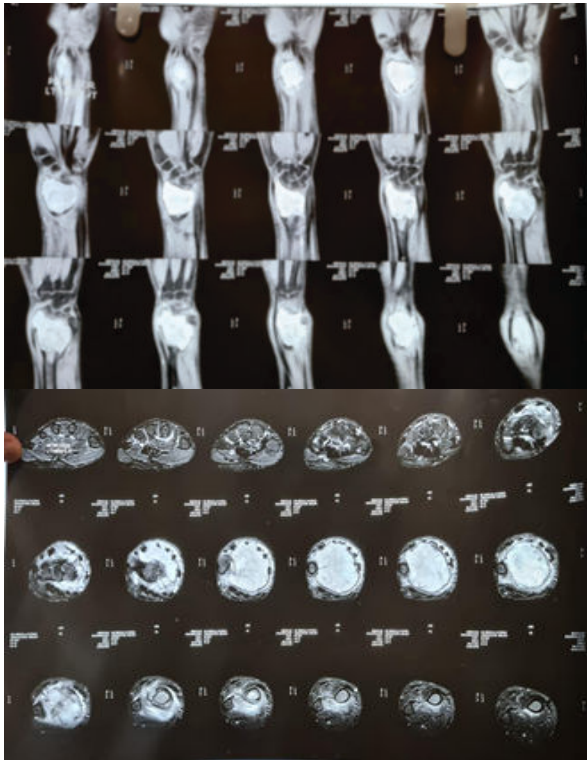
A case of giant cell tumour of distal radius was confirmed by further investigations **X-ray**-Aggressive, eccentric, expansile, osteolytic lesion present at epiphysis extending to metaphysis in the left distal radius, approximately measuring around 7 x 3 cm. The transition zone was narrow, with a cortical breach in the metaphyseal region and subchondral bone destruction. However, there was a minimal periosteal reaction.



Pre-op Xray

MRI-MRI was used to evaluate the extent of the lesion, its extraosseous component, its relation to the neurovascular bundle and to place the level of transection of the bone including 1cm of healthy cortical bone.





MRI of left wrist joint showing GCT of the distal radius

Histopathology Report- core needle biopsy was done, which showed mononuclear stromal cells with scattered osteoclast like giant cells.

Pre-operative Planning

- Pt was given 3-doses of Denosumab pre-operatively -120mg subcutaneously every 15 days apart along with supplementation of calcium and vitamin-D3 over 2 months with regular monitoring of serum calcium levels.
- En-bloc excision of the tumour with ipsilateral ulnar translocation and wrist arthrodesis with pre-contoured 3.5mm locking plate was planned.
- We examined the complications of the technique, the time taken to union and the functional outcome. The functional status was determined at the follow-up using the Musculoskeletal Tumour Society Scoring System (MSTS). This was based on the analysis of three factors of pain, functional activities and emotional acceptance, pertinent to the patient as a whole, and three specifics to the upper limb namely positioning of the hand, manual dexterity and lifting ability. For each of the six factors, values of 0 to 5 were assigned based on established criteria. The result was expressed as a sum total with a maximum score of 30.

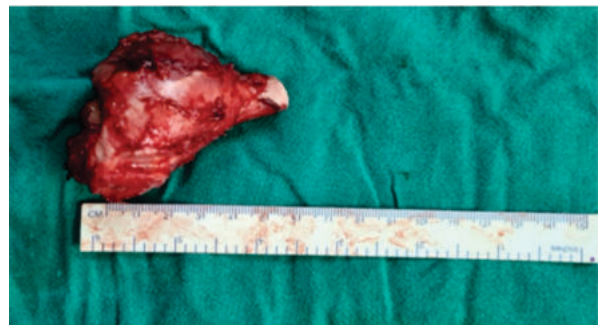
Operative Technique

Under general anaesthesia, patient is lying in supine position with left upper limb on the side table in complete extension and forearm in pronation. Under tourniquet control, Skin incision is marked on the dorsal side of the wrist with marker with incision centring over the tumour, extending proximally over the radius to centre of 3rd metacarpal distally. The proximal margin of tumour was marked as per preoperative planning and resected. Articular surfaces of distal ulna, scaphoid and lunate were freshened for arthrodesis. Around 8 cm of the distal ulna was resected, keeping intact all soft tissue attachments. Before transposing the ulna, care was taken to ensure that the periosteal sleeve had been completely divided around the ulna at the level of the proximal osteotomy and resected ulna is centralized between the lunate column and the radius's cut end. Without disrupting the retained muscle attachment, the ulna should be transposed at the defect created after tumour removal at the distal radius. The transposed ulna was aligned with the radius and the third metacarpal so that the forearm retained full pronation and supination. Internal fixation was done with pre-contoured 3.5mm dynamic locking compression plate(13-hole). Thorough wash was given. Skin was closed in layers over a drain. Wrist was immobilized in below elbow slab for 2 weeks until suture removal.



Operative image-Marked skin incision.

Intra-op image- soft tissue exposed and void seen after en bloc excision of the tumour.



Intra-op Images Of The Excised Tumour.

RESULTS

Post-operatively patient was followed up at 2 weeks, 6 weeks, 12 weeks and monthly up to 6 months. There were no clinical and radiological sign of recurrence. Denosumab treatment was

administered for 2 months pre-surgery; it was generally well tolerated and the patients had no treatment-related adverse events. At the final follow-up, we assessed the functional outcome with Musculoskeletal Tumour Society (MSTS) scoring system. The patient had a range of 60 degrees of supination and 90 degrees of pronation. Patient had MSTS score of 26/30 at 6 months follow up.



Post-op Xray on day 1



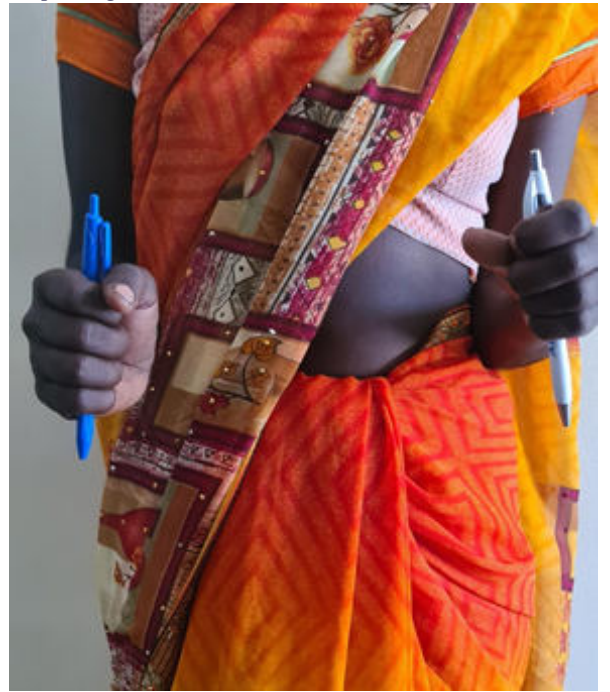
Post-op Xray at 6 weeks

Post-op Xray at 12 weeks



Post-op Xray at 6month

Grip Strength



Pronation





Supination

DISCUSSION

GCT of distal radius affects young patients with relatively normal life expectancy so it's tough for management and rehabilitation.

The origin of pain in GCTB is multifactorial including mechanical stress from tumour related pressure, tumour growth with expansion of the periosteum, the loss of structurally significant bone and mechanical failure. The production of prostaglandins, endothelin and other noxious factors by the tumour cells are also known to result in pain. In all patients a decrease in wrist pain and improved wrist function was noted within 2 months of commencing denosumab therapy.^[38] Local recurrence and loss of joint function are challenging task to control in GCT surgery. Curettage and filling of void with bone graft or bone graft helps to achieve wrist function but is having very high chances of local recurrence (30–50%)^[14,26,28-32] Denosumab applied as a preoperative neoadjuvant to delay or stop the progression of GCTB and to create a sclerotic bone rim making the tumour well-demarcated. It also converts an inoperable tumour to a resectable one by shrinking the extra-osseous component and ossifying tumour.^[11,33] This approach allows for less bone resection and increases the possibility of achieving complete excision with extended curettage, even in previously unresectable lesions.^[34] First, as was observed in surgery, the blood supply of tumours and the surrounding tissue decreased considerably, which simplified the procedure. Second, the newly formed osseous rim after denosumab made it easier for the surgeon to identify the safe margin, therefore decreasing the possibility of injury to important adjacent neurovascular structures. Third, the increased tumour density facilitated effective separation with less concern about inadvertent tumour cells spilling.^[12,35,36,37] Reconstruction after excision of the distal radius for GCT is a challenge because of the high functional demands on the hand, the limited surrounding soft tissue, the proximity of adjacent nerves and tendons and the young age and relatively long-life expectancy of this group of patients^[18] Various factors need to be considered when evaluating a technique of reconstruction. These include the ease of the procedure, its morbidity, the complications and functional outcome and the durability of the reconstructed segment. Various treatment options available include En-Bloc resection of the lesion and reconstruction with ipsilateral proximal fibula autograft (vascularized/non-vascularized), tri-cortical iliac graft, structural allografts, distal ulnar centralization, etc.^[21]

The use of a free nonvascular proximal fibular graft to replace the resected distal radius was described by Mays et al.^[39] In these cases, problems such as non-union (12-38%), fracture of graft (13-29%) and risk of infection are not uncommon^[20]. The increased operative time, non-union and additional comorbidity to the donor area are other limitations.

Ipsilateral ulnar transfer is an easy, inexpensive technique. It is also quicker to perform than free vascularised fibular grafting. Since the surgical procedure is restricted to the same limb, morbidity is reduced. The shorter surgical procedure and the fact that a graft which retains its

blood supply has been used possibly help to reduce infection, helps in early bone union and maintains good finger strength^[15,40,41,42]

Ensuring that the periosteal sleeve has been completely divided at the level of the ulnar osteotomy may prevent postoperative radio-ulnar synostosis. Failure to divide the proximal periosteum circumferentially causes it to shear off from the end of the divided ulna as it is being transposed. This may not only impair the vascularity of the transposed bone, but may result in the formation of bone along the retained periosteal bridge thereby leading to radio-ulnar synostosis and limiting rotation of the forearm. The stable fixation also enabled us to use a below-elbow splint which allowed early active movement of the shoulder, elbow and fingers. Even though there is a one-bone forearm, the preservation of pronator teres attachment in the ulna helps in pronation, and biceps along with the supinator acting as a forearm supinator. Hence, this procedure conserves rotation. The tumour's local recurrence is not dependent on the reconstruction technique, but meticulous En bloc excision without tumour spillage in the wound. The translocated distal ulna acts as a vascularized graft in this surgery.^[23,24,43]

CONCLUSION

Pre-operative denosumab therapy makes subsequent surgery more feasible by surgical down-staging of the tumour to a less morbid surgical salvage procedure allowing for improved patient function. It also helps in complete excision of the tumour with no surgical spillage during resection due to hardened osteosclerotic rim around the tumour. Ulnar translocation is an easy, inexpensive method of reconstructing the distal end of the radius after excision for a GCT. It avoids the need for a microvascular procedure and gives excellent rotation of the forearm and function of the hand.

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