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Rare Case of an Unresectable Giant Cell Tumor of Pubic Bone

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Abstract

Giant cell tumor (GCT) of bone, a benign but locally aggressive invasive tumor. It commonly affects long bones, has a low incidence in pelvis (1.5-6.1%). It is most commonly treated with a surgical approach. However, here we present a rare case of GCT of pubic bone, which was rendered unresectable due to its location and extensive nature. Thereby, treated with radical radiation therapy and injection denosumab.

Introduction

Giant cell tumor is a primary bone tumor with more common incidence in females than males [1]. It is a benign but locally aggressive and invasive tumor, which rarely metastasizes to lungs [2]. It usually affects skeletally mature adults, 20-40 years of age. It usually arises in the epiphysis or epi-metaphysical junction of long bones with the most common site being distal femur and proximal tibia [3]. Rarely, it affects skeletally immature children, where it arises from the metaphysis [3]. Less commonly, it may affect craniofacial bones, vertebral body, sacrum, hand and feet bones. It rarely affects the pelvis (with an approximate 1.5-6.1% of incidence) [4-7]. Diagnosis is confirmed by histopathological examination. The most commonly recommended treatment for giant cell tumors (GCTs) of bone consists of intralesional procedures such as curettage, and filling of the defect either with bone grafts or bone cement,with wide local excision done to reduce the recurrence rate [8,9].

Case description

A 38 years old female, with h/o hypothyroidism (since 27 years), presented with complaints of pain and swelling in pubic area, which was gradually increasing in intensity with difficulty in movement of left thigh since 6 month before presenting to the clinician in Feb, 2022. All routine blood investigations we within normal limits. X-ray pelvis suggested a growth in left pubic bone with extending to right side. PET-CT (17.02.2022) revealed a large lobulated destructive mass with the associated soft tissue component showing increased uptake (9.6×8.3×10.1cm) involving bilateral pubic bones. Associated soft tissue component infiltrating left obturator internus muscle, extending to medial compartment of left proximal thigh with contour bulge. Medially, displacing the pelvic contents to right side and indents the urinary bladder. CT guided biopsy from left superior pubic ramus (17.02.2022) revealed giant cell rich lesion, favoring giant cell tumor. It was classified as grade III according to Campaanacci's classification [10]. CEMRI Pelvis (22.02.2022) revealed a 9.5×8.5×11cm expansive destructive soft tissue mass lesion involving left pubic bone, left superior pubic ramus and small portion of left inferior pubic ramus.

The extra osseous soft tissue component extending to left hemipelvis in the infra lavatory compartment involving the obturator internus muscle with the medially projecting nodular collar stud, abutting the urethra and lower vaginal walls inferiorly extending to upper medial left thigh in the intramuscular space (till 3 cm below the level of lesser trochanter). In view of its location and its extensive nature, it was considered unresectable. After multidisciplinary discussion in tumor board, the patient was planned for radical radiation therapy to pelvis to a dose of 60 Gy

in 30 fractions along with injection denosumab 120mg subcutaneously per month. The patient received external beam radiation therapy to the left pelvis on linear accelerator to a dose of 60 Gy in 30 fractions (daily once, 5 days a week) from 22.03.2022 to 16.05.2022. Following which, patient was continued on monthly inj Denusumab, 120mg subcutaneously.

Initially there was only mild relief in symptoms. On follow up imaging, CEMRI pelvis (28.07.2022) revealed no significant change in the size of the bony lesion in pelvis, but predominant necrosis present, suggesting partial response to treatment. Patient gradually started to improve symptomatically in Aug, 2022. Patient received 5 cycles (monthly) of inj denosumab, 120mg subcutaneously. PET-CT (16.03.2023) suggested expansive bony mass, with mild reduction in size and FDG avidity with progressive peripheral sclerosis, suggesting response to therapy. Presently patient has significantly recovered with no complaints of pain or swelling in the pubic area. She has no difficulty in movement and is able to carry out routine activities well. On examination, no mass is felt with no local signs of progression. These features correspond to good response to treatment (Figures 1-4).

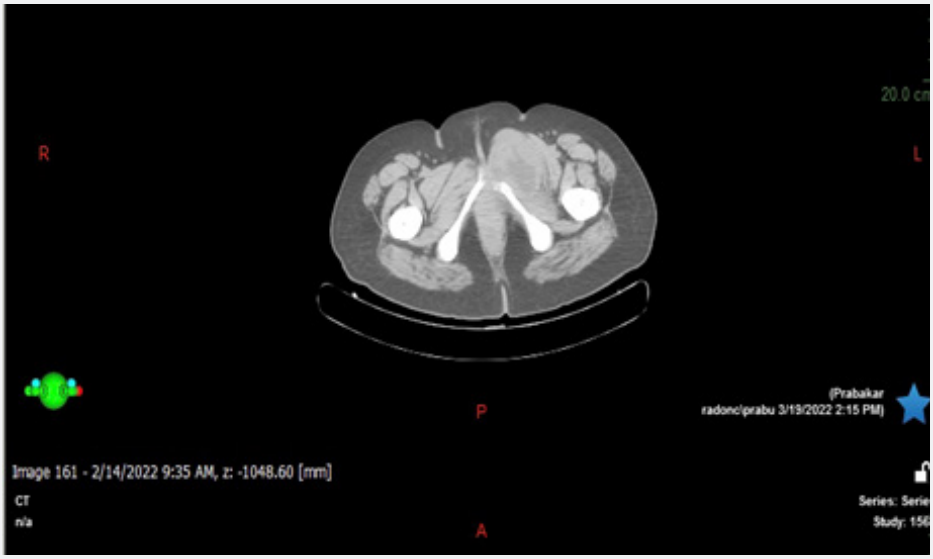

Figure 1A: Positron emission tomography (PET) computed Tomography (CT) showing soft tissue mass involving the bilateral pubic bones (pretreatment).

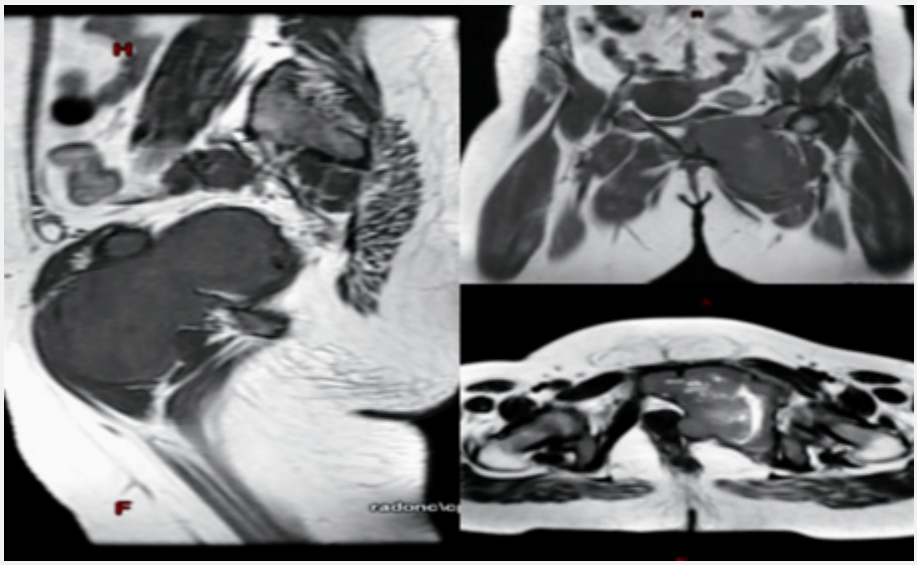

Figure 1B: Contrast enhanced MRI pelvis (Diagnostic).

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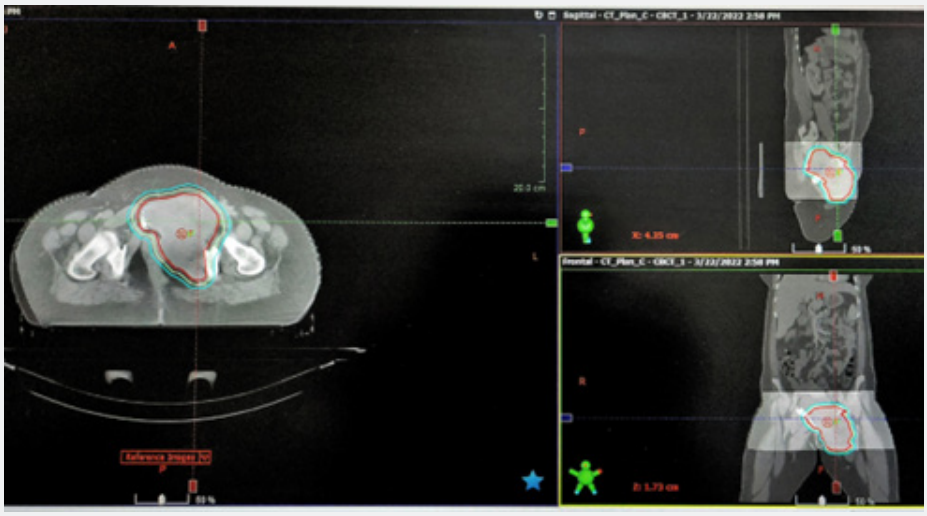

Figure 2: Treatment planning volumes. Gross Tumor Volume (GTV) (Red), Clinical Target Volume (CTV) (yellow), Planning Target volume (PTV) (green).

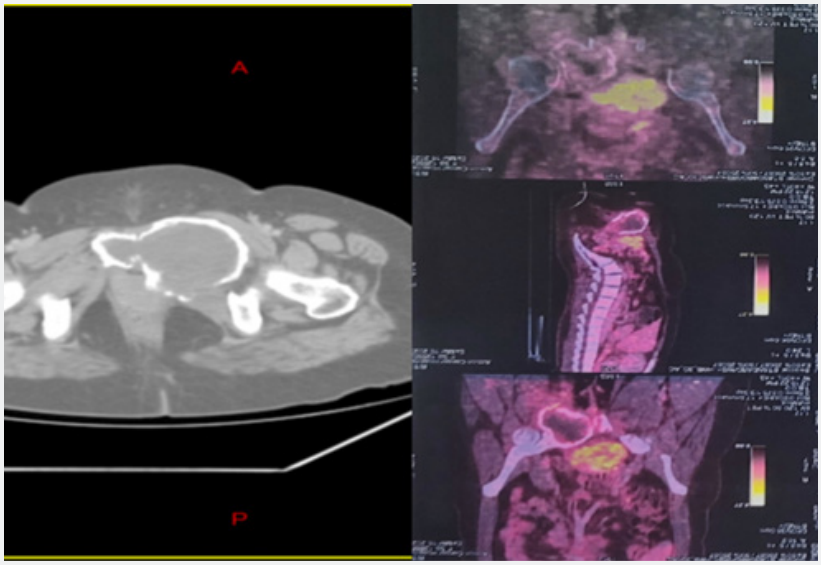

Figure 3: Positron emission tomography (PET) computed Tomography (CT) showing soft tissue mass involving the bilateral pubic bones (post-treatment).

Discussion

Giant cell tumor is a benign, but locally aggressive and invasive tumor, commonly affecting the young adults. It mostly affects long bones of extremities, treated with radical surgery with 80-90% of local control [11-13]. Local control rates decrease with the involvement of axial skeleton. For tumors located in extremities, surgery is the usual treatment with 80-90% of locoregional control rates. But, the probability of successful surgical therapy decreases in axial skeleton [14]. Although, historically GCTB was considered radioresistant, with advancement in treatment techniques and achieving better dose delivery and coverage, radiation therapy is considered as an effective treatment nowadays, especially in unresectable tumors [15,16]. Use of mega voltage radiation therapy has shown significant local control rates with minimal side effects.

Wlodzimierz Ruka et al. [17] analyzed 122 patients treated with RT for unresectable giant cell tumor of bone (GCTB). This is the largest study of patients treated with RT for GCTB. In this study, patients that were not appropriate candidates for surgery, received radical radiation with doses ranging from 26 to 89 Gy. Local control rates were 84% and 5- and 10-year local progression-free survival (LPFS) was 83% and 73% respectively. 5- year

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LPFS rates were 70.5% for the axial skeleton location vs. 88% for peripheral bones location [17]. Jan Kriz et al. analyzed 35 patients from six co-operating German institutions, from 1975 to 2010. 19 patients received RT for recurrent or unresectable disease and 16 patients for non-in-Santo resection. The 5-year overall survival and disease-free survival rates observed were 90% and 59% respectively. 5-year local control and distant metastasis-free survival rates observed were 60% and 89% respectively. Radiation doses ranged from 35 to 60 Gy [18]. No sarcomatous transformations or malignancies were observed, which is the major concern when GCTB is treated with RT [18].

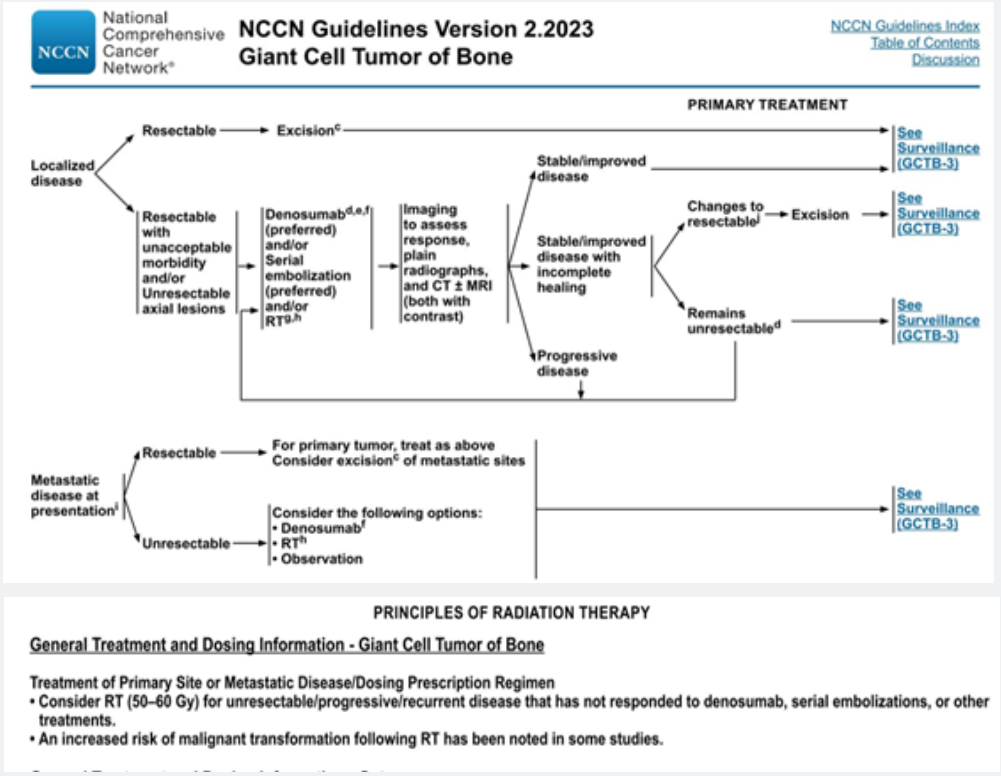

Figure 4: NCCN guidelines for management of giant cell tumors.

Recommendations regarding radiotherapy dose and fractionation schedules vary. Bennet et al. [19] and Chen et al. [20] recommend a total dose of at least 40 Gy for optimal local control. Harwood et al. [21] and Malone et al. [22] suggest a dose of 35 Gy in 15 fractions over 3 weeks as a safe and effective treatment regime. However, MK Nair et al. [23] recommended a dose of 45 Gy in 15–20 fractions over 3–4 weeks. In our case, a patient was treated with radical radiation therapy to the left pelvis on linear accelerator to a dose of 60 Gy in 30 fractions. Along with monthly injection denosumab 120mg, subcutaneously. Denosumab is a monoclonal antibody, which inhibits the function of RANK (receptor activator of nuclear factor NF-kB) by binding to RANK ligand, thereby inhibiting osteoclast formation [24]. There was gradual improvement in patient symptoms with least treatment related side effects, suggesting adequate response to treatment.

Conclusion

Giant cell tumor rarely involves the pubic bones (1.5-6.1%). This case illustrates the involvement of pubic bones which could not be excised. Therefore, treated with radical radiation therapy and injection denusumab. Radiation is an easy, safe and effective treatment option, even as the sole treatment modality for patients with recurrent and unresectable GTCB. Therefore, can be considered an adjuvant to surgery or as alternative therapy in cases of GCTB that are unresectable or in which excision would result in substantial functional deficits, with minimal treatment related side effects.

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