Clinical Oncology: Case Reports

Case Report

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Bone Marrow sparing VMAT in Whole Lung Irradiation

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Abstract

Background: Acute hematological toxicity is one of the side effects of whole lung irradiation(WLI) leading to interruption of treatment. With the novel radiotherapy techniques like Volume Modulated Arc Therapy (VMAT) it is possible to minimize treatment associated hematological side effects by sparing bone marrow. We report a new technique of Bone Marrow sparing VMAT (MS-VMAT) for WLI.

Case Representation: We describe a 20-year male resident of Iraq, diagnosed as Giant cell tumor with pulmonary metastases, planned for 28.8 Gray/16 fractions to lung parenchymal nodules and 24 Gray/16 fractions to bilateral whole lungs using standard VMAT. After 7 fractions of radiotherapy patient developed Grade III hematological toxicity for which new plan was made with MS-VMAT. We generated three plans using standard anteroposterior-poseroanterior (AP-PA), VMAT and MS-VMAT. Dosimetric advantage was observed in MS-VMAT over standard VMAT technique in terms of minimizing dose to bone marrow. Bone marrow sparing VMAT showed more sparing of marrow in vertebrae and sternum thereby minimizing the Grade III hematological toxicity.

Conclusion: Effective bone marrow sparing may be possible with bone marrow sparing VMAT. Large scale randomized trials are needed to validate our results.

Keywords

Marrow sparing Volume modulated arc therapy (MS-VMAT); Whole Lung Irradiation (WLI)

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Introduction

Giant cell tumor of bone (GCTB) is amongst rare, benign but aggressive bone tumors, typically seen in young adults. Despite the benign nature, the spectrum of GCTB is highly variable and unpredictable. In approximately 2 to 3 % of patients, metastases occur, more frequently in lung. The pulmonary metastases(mets) behave differently compared to mets from other solid tumors or sarcomas, because of is benign nature. The pulmonary mets have been designated as benign pulmonary implants [1]. The choice of therapy for pulmonary mets depends upon symptoms, progressive nature of disease and patient's performance status. Whole Lung irradiation (WLI) is advocated for patients whose pulmonary mets are unresectable, who decline thoracic surgery or who progress after surgery [2]. Traditionally, WLI was performed using AP-PA fields.

With the use of modern radiotherapy technique like VMAT, the dose to the organs at risk (OAR's) like heart and bone marrow can be reduced, compared to AP-PA field technique. In adults, the red bone marrow is present in sternum, ribs, scapula, vertebrae and pelvis, thereby exposing large volume of bone marrow to radiation. However, we report a case who showed acute marrow suppression while receiving VMAT technique-based WLI this necessitated a change in the radiotherapy plan using MS-VMAT technique. To the best of our knowledge, this is a first report on Bone Marrow sparing VMAT for WLI.

CASE REPORT

A 20years Iraqi male, diagnosed to have swelling over left shin for which he underwent debridement surgery in Iraq in August 2015. After 2 months he developed regrowth of local swelling and underwent 2nd debridement and placement of two metallic rods to support tibia in Oct 2015 at Iraq. In February 2016, he came to India for further treatment, on referral from his surgeon, but his medical records were incomplete. A biopsy from the surgical site of Left Fibula was suggestive of Cellular Fibrous Histiocytoma of bone. He underwent Dufourmentel Fasciocutaneous flap + Split skin graft (SSG) of left leg to avoid amputation in February 2016, but the swelling persisted after flap surgery. He was then counselled regarding the aggressive nature of his disease and consented to undergo Left above knee amputation in December 2016.Post Op Histopathology was suggestive of Giant cell tumor of bone. Tumor cells expressed vimentin Bcl2, CD99, CD68, p63 and Ki-67-16%. In June 2017 he complained of back pain. Whole body Positron Emission Tomography (WBPET-CT) revealed a solitary D8 lesion, with one non-avid sub-centimeter nodule in right lung basal region. For this, he underwent excision and vertebroplasty. Post op histopathology was suggestive of pleomorphic undifferentiated sarcoma compatible with mets of GCBT. A tumor board decision was made to observe the right lung nodule. Post-operatively, he received Denosumab and Zoledronic acid for 4 doses. Additionally, in view of the solitary mets in spine, local radiotherapy dose of 45Gy/20Fr/4weeks to D-8 vertebra site was delivered in July 2017. Three months later, follow-up WBPET-CT in October 2017 showed two non-avid rounded fibro-nodular lesions, one in posterior basal segment of right lower lobe and another lateral basal segment of left lower lobe. Larger lesion located in right lung base measured

2.4x 1.7cm, as compared to prior sub-centimeter size. He underwent VATS assisted B/L Metastasectomy (Pulmonary) in January 2018, following which he received adjuvant chemotherapy. WBPET-CT done in August 2018 was suggestive of interval appearance of 5 new sub-cm size lung nodules (B/L). D-8 spine lesion site remained non-avid, non-active. Patient was given option of high dose methotrexate (HDMTx), but he was unwilling for the same due to reasons of finance and stay in India and wanted to come after some time for HDMTx. Repeat WBPET-CT in February 2019 was suggestive of no change compared to previous WBPET-CT. Patient received three cycles of HDMTx in February 2019. Contrast Enhanced Computer Tomography (CECT) Chest was done in October 2019 which was suggestive of bilateral lung parenchymal small soft tissue nodular lesions, seven in number. Lytic areas within D8 vertebral body was likely due to post vertebroplasty/ interventional status, and appeared non-active again. As compared to WBPET-CT done in February 2019, this CECT showed significant increase in number of subcentrimetric to centrimetric lung parenchymal nodules. In view of progressive nature of disease and unresectability, patient was given option of WLI. All the radiation procedure, side effects and prognosis was explained and an informed written consent was taken before starting treatment.

Radiotherapy treatment planning and delivery

Immobilization mould for the patient was prepared in supine position with arms overhead using wing board. CT simulation was done with 3mm slices from mandible to pelvic brim using breath hold technique. Clinical target volume (CTV) of both lungs was contoured to cover the entire three-dimension bilateral lung(B/L) volume. Planning target volume (PTV) was same as CTV for WLI as breath hold with Image guidance used. The pulmonary nodules were identified and contoured separately for boost. OAR's contoured were heart, sternum, vertebral body and liver. Patient was planned for B/L whole lung irradiation to total dose of 24Gy/16Fr/3weeks and boost to parenchymal lung nodules for total dose 28.8Gy/16Fr/3weeks using VMAT. Daily fraction was 1.5Gy for WLI and 1.8Gy for the boost, as simultaneous integrated boost(SIB). VMAT plan was generated with Eclipse v15.5 treatment planning system (Varian Medical systems, Palo Alto,CA,USA), with AAA algorithm. The goal was >98% of PTV should receive >95% of prescribed dose and <2% PTV should receive >110% of the prescribed dose. Dose volume constraints were as per QUANTEC. Treatment was planned with two full 360 degree arcs of VMAT. A total of 400 monitor units was needed to deliver the plan. After 7Fractions of WLI, he had fall in total leucocyte count, and his absolute neutrophil count(ANC) was 300/mm3(NCI risk category 4). RT course was interrupted for four days and patient was managed conservatively with granulocyte-colony stimulating factor(G-CSF) Inj Neukine 300mcg OD for 3days along with oral Levofloxacin 750 mg once daily for 5days. In view of Grade III hematological toxicity the initial plan was re-evaluated. Radiation therapy planning was re-evaluated and modified. With the aim to spare bone marrow we contoured the ribs, sternum and vertebrae, to generate a new plan to spare bone marrow within the B/L WLI irradiation volume. This new plan had spillage of dose to lateral structures and heart because the treatment planning system was trying to spare the ribs. In view of this, we contoured only the sternum and vertebral body and generated a new plan for bone marrow sparing VMAT(MS-VMAT). Dosimetric advantage of bone marrow sparing was seen with this plan. He received remaining 9 Fractions to complete the RT course with the MS-VMAT. To compare VMAT, MS-VMAT and AP-PA fields technique, we generated a standard AP-PA field plan using two equally weighted beams with the same 6MV (megavolts) of photons (as used for VMAT and MS-VMAT), with >95% PTV receiving >95% of prescribed dose. For PTV, homogeneity Index (HI) was used for comparison of the three plans. HI was calculated as (D2%-D98%)/ D50%. The dose to OAR's and HI is listed in (Table 1).

Table 1: Comparative dose to structures in the 3 plans generated for this case of WLI.

Structure	VMAT Non sparing	MS sparing VMAT	AP-PA
PTV D2 (Gy) D95 (Gy) D98 (Gy)	 26 23.9 23.6	 26.4 23.7 23.2	 27.28 22.96 22.2
Heart (Dmean)	15.4	18.4	23.6
Liver	10.1	12.2	11.2
Ribs (Dmean)	20.3	19.1	22.2
Sternum (Dmean)	20.7	11.9	24.6
Thoracic Vertebrae (Dmean)	21	12.5	17.5
Bone Marrow (Dmean)	21.4	10.9	18.3
Homogeneity Index	0.1	0.13	.19

Dose distribution of the three plans. We compared the DVH of the Bone Marrow of the three plans.

We confirm dosimetric advantage of VMAT over AP-PA field technique, while there is advantage of Bone Marrow sparing VMAT to prevent acute Grade III hematological toxicities

Quality assurance of treatment

The calculated VMAT plan was verified prior to treatment using Octavius 3D. Daily cone beam computer tomography (CBCT) was taken.

Clinical Outcome

He completed his treatment in November 2019 and returned to India for the first follow up in March 2020. His complete blood counts done in December 2019 and March 2020 was within normal limits. PET-CT done in March 2020 was suggestive of stable disease.

Discussion

In patients with GCT with pulmonary metastases, radiotherapy given if patient refuses for surgery, or, has unresectable or progressive pulmonary metastases post chemotherapy. Whole lung irradiation used very frequently for treating pulmonary metastases in Ewing's sarcoma. It's less frequently used in GCT patients with pulmonary metastases [2]. We report a novel case of Bone marrow sparing VMAT in a patient with whole lung irradiation to prevent Grade III hematological toxicity. The mechanism of decreased bone marrow toxicity is not fully understood, but sparing bone marrow may be a contributing factor leading to lower rates of neutropenia. This case report has some limitations. Firstly, since it is a single case report on a patient with short follow-up, a large randomized trial is needed to validate our results. Secondly, due to low dose leakage to the normal tissues, there may be risk of secondary malignancy, hence long follow up is necessary. We suggest using Bone marrow sparing VMAT for patients with pulmonary metastases to prevent acute hematological

toxicity and further randomized trials can validate our suggestion.

Conclusion

Bone marrow sparing VMAT may be considered by radiation oncologist for preventing acute hematological toxicities.

References

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