Journal of
Cancer Research and Molecular Medicine

Open Science Publications

Volume 5, Issue 1 - 2024

www.opensciencepublications.com

Adjuvant Radiation in Malignant Peripheral Nerve Sheath Tumor

Case Report

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Article Information: **Submission:** 19/01/2024; **Accepted:** 06/02/2024; **Published:** 08/02/2024

Abstract

Malignant peripheral nerve sheath tumor (MPNSTs) are highly aggressive soft tissue sarcomas for which surgical resection is the mainstay of therapy. However, recurrence rate is high and there are very few options for refractory or metastatic MPNST. Many studies have stated that the use of adjuvant therapy is expanding when patients do not have clear surgical margins. In this report we discuss a case of MPNST which had complete response following adjuvant radiation.

Keywords: Nerve Sheath Tumor; Radiation; NF1

Introduction

Malignant peripheral nerve sheath tumour (MPNST) arises from or differentiates toward cells of the peripheral nerve sheath. They account for about 10% of soft tissue sarcomas [1,2]. Normal nerve sheath consists of Schwann cells, perineurial cells and mesenchymal cells such as fibroblasts, endothelial cells, pericytes, and epineurial lipocytes. The majority arise *de novo* in normal peripheral nerves or from neurofibromas; only rare examples arise in schwannoma, ganglioneuroma, orpheochromocytoma. No differentiation may be apparent in high grade tumors. Occasional MPNSTs show Ultrastructural or immune histochemical features of fibroblasts or perineurial cells. No differentiation may be apparent in some high grade tumors. Occasionally they show Ultrastructural or immunohistochemical features of fibroblasts or perineurial cells. Therefore, the noncommittal term MPNST is preferred, acknowledging the possibility that these tumors may be histogenetically diverse [25]. Complete surgical resection is the mainstay of treatment. However, in view of high rates of recurrence, refractory or metastatic nature, adjuvant treatment is advised. Despite multimodality therapy comprising of surgical resection, chemo-radiotherapy, the 5-year survival ranges from 35 - 50%. [3, 4]

Irradiation has significant impact on local control. Wong et al reported that 5-year local control is 73% when cumulative radiation dose exceeded 60 Gy, compared with 50% for lesser doses, proving that postoperative radiation plays a role in the management. [1] When brachytherapy was given along with external beam radiotherapy, the 5-year local control is 88%, compared with 51% in those who received external beam only when close surgical margins were involved. Stucky et al encouraged that radiation therapy be utilized for tumors that have aggressive features such as size 5 cm, high grade, and R1 or R2 margin status [11]. We present the treatment of MPNST in the neck treated by surgical resection followed by adjuvant radiotherapy, which led to excellent oncological outcomes.

Case Presentation

A 45year old gentleman was evaluated for swelling on the left side of the neck. CT scan of neck showed ill-defined heterogeneously enhancing lesion of size 51x45mm. Patient underwent wide

local excision and left Modified Radical Neck Dissection type II. Postoperative histopathology reported as malignant peripheral nerve sheath tumor-pT2N1.

Neurofibromatosis is an important risk factor for MPNST as 50–60% of the tumor occurs in those with NF-1 as they have a somatic mutation in the NF1tumor suppressor gene, resulting in the development of benign nerve sheath tumors (plexiform neurofibromas) which are prone for malignant degeneration.

However, our patient did not show features suggestive of NF-1 and had no history of radiotherapy, suggesting a sporadic occurrence.

Radiation Therapy

Thirty days post-surgery, after wound healing, patient was taken up for radiotherapy. Immobilization was done with a thermoplastic mask on an indexed carbon fibre flat top and simulated with Siemens Soma tom. Go. Now which is a 16 slice CT machine with a 70 cm bore. A CT image of 3 mm slice thickness was acquired from vertex to T6 vertebra. For Target volume delineation, the clinical target volume was the postoperative tumour bed with margins including the submandibular to supraclavicular area, accounting for the subclinical microscopic disease spread and the planning target volume accounting for setup error during everyday treatment.

Treatment Planning

Radiotherapy was planned by 3D Conformal RT technique with two parallel opposed fields, in the anteroposterior and vice versa to the upper fields with a single isocentre to avoid the beam entry and exit to the contralateral region. A single direct field to the supraclavicular region with a collimator rotation of 10^0 to avoid the exit dose contribution to spine was used. For uniform dose distribution, wedges were used with a wedge angle of 15^0. Apex of the lung received minimal exit dose. Treatment plan was evaluated for 95% of the target coverage with the prescribed dose. The doses to the Organs at Risk (OARs) are limited as follows: Spine Dmax < 15.15 Gy and Ipsilateral Parotid with a Mean dose < 26 Gy. The prescribed dose of 60 Gy is delivered in 30fractions with 6 MV photons.PET CT scan after 6 months of follow up reported complete response with no residual tumour in the patient

Discussion

The role of radiotherapy in the management of soft tissue sarcoma has changed dramatically over the last30 years. Initially, these tumors were deemed "radio resistant" and surgical resection was the only treatment modality until a study by McNeer et al. and Suitet al, who treated Unresectable patients with definitive radiotherapy questioned the long-held belief of "radio resistance "of these tumors [5-7] .Yang et al. reported that postoperative radiotherapy is effective for local control in soft tissue sarcomas of the extremities.[8,9] Irradiation showed to have a significant impact on local disease control where the cumulative radiation dose gave a 5-year local control rate of 73% when the dose exceeded 60 Gy. The use of IOERT (Intra operative electron radiotherapy) or brachytherapy in addition to external beam radiation also improved local control of disease. For patients who received IOERT or brachytherapy, the 5-year local control rate was 88%, compared with 51% for those treated with external beam only.

Complex anatomy of the neck poses challenges in the treatment such as in complete resection that are associated with risk of residual disease and local recurrence. It also hinders delivery of high radiation doses owing to the proximity of tumor to surrounding vital structures. This can bead dressed by using immobilization techniques for accurate reproducibility in positioning of patient, set-up verification paired with meticulous planning to ensure precise radiation delivery [10] .The introduction of RT modalities like Image Guided RT, intensity modulation RT, volumetric modulated arc therapy, stereotactic RT, and proton based RT has revolutionized radiotherapy by precise delivery of large doses of radiation to the tumor and also reducing toxicities providing an organ sparing approach. Multiple factors have been documented as prognostic factors for MPNST. As seen in the literature, age at diagnosis has been a prognostic factor for some studies including Wanebo et al. who found that there was reduced survival in patients younger than 30 years of age reflecting on the aggressiveness in the younger population [12]. Some studies have shown that NF1 is a poor prognostic factor for survival statistically while others have shown a trend toward sporadic tumors being a good prognostic indicator. The 5-year survival rates of those with NF1-associated tumors ranged from 16 to 60%, whereas in sporadic tumors the rates ranged from 47 to75%. Tumour location has been hypothesized as a prognostic factor because of the ability of complete surgical resection to be more easily achieved in extremities versus tumors in the abdomen or chest [13-17]. It was also easier to achieve a negative surgical margin for tumor in extremities as compared with other sites. Sordillo *et al.* also reported significantly better survival in patients with MPNST of the extremities.[17] Although some studies report that radiotherapy has no impact on survival [18-24] several studies have shown that radiotherapy achieves margin control and prolongs survival in soft tissue sarcomas [18-24].

Limitation

Short duration of follow up of the patient. Regarding the radiation technique, 3D Conformal radiotherapy is optimally made use of for this specific case. However, high precision radiotherapy can also be considered on an individualised basis.

Conclusion

Postoperative radiotherapy can help to achieve good response in MPNST.

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Citation: Venkatesh Prasad PM, Valas S, Palanisamy K, Subramanian VS, Keerthana A, et al. Adjuvant Radiation in Malignant Peripheral Nerve Sheath Tumor. J Cancer Res Molecul Med. 2024;5(1): 106.

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