Role of Proton Beam Therapy in Spinal Chordomas: A Narrative Review of The Literature

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Abstract

Chordomas are rare malignant neoplasms arising from vestigial remnants of the embryonic notochord. Approximately 55-70% of chordomas develop within the vertebral column. Their affinity to develop within the bones of the axial skeleton and propensity to locally invade and recur makes them challenging candidates for complete surgical excision. Adjuvant therapies are hence necessary to improve outcomes; for which chemotherapy has been observed to be largely ineffective, owing to the tumour being resistant to it. Radiotherapy is the current adjuvant therapy of choice for chordoma management. Over the years, proton beam therapy (PBT) has been the subject of medical attention, given the dosimetric benefits it confers over traditional radiotherapy, allowing more concentrated radiation to be given to the target of interest and reducing damage to surrounding normal tissue. A review of the current literature reveals PBT offers significantly better outcomes when used as an adjuvant to maximal surgical resection rather than as a definitive therapy.

Keywords: Chordoma, Proton Beam Therapy, Outcome, Recurrence, Spinal, Adjuvant Therapy

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Introduction

Chordomas are rare malignant neoplasms arising from vestigial remnants of the embryonic notochord.[1] They are mostly intra-osseous and affect the axial skeleton, with 35%-40% presenting in the skull base,40%-50% in the sacrococcygeal region and 15%-20% in the vertebral bodies.[2-4] Chordomas have an invasive nature and a propensity to recur which, when combined with their affinity to afflict the axial skeleton, makes them difficult candidates for complete surgical excision, hence necessitating adjuvant treatment.[2,3,5] Given the resistance of chordomas to chemotherapy, radiation is the ancillary treatment modality commonly used to augment surgical excision of chordomas.[3]

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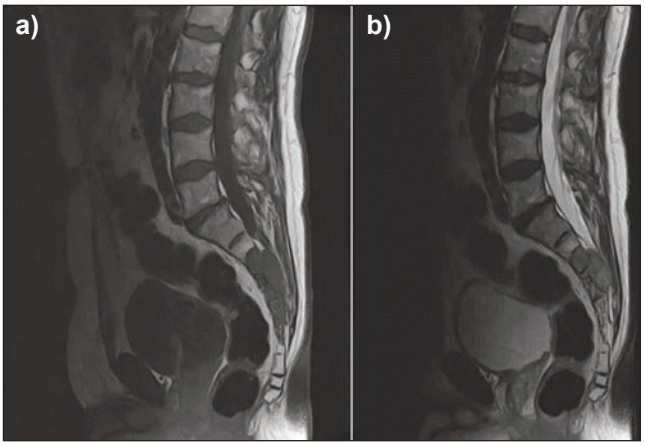

Figure: MRI Lumbosacral Spine Saggital View of a patient with a sacral chordoma; a) T1 weighted image without contrast – sacral chordoma can be seen as a hypointense lesion affecting the S2-S5 vertebrae. b) T2 weighted image without contrast – sacral chordoma can be seen as a hyperintense lesion affecting the S2-S5 vertebrae.

Proton beam therapy (PBT) is a radiotherapy modality that uses beams comprising protons to deliver radiation to tissues.[6] This narrative review attempts to summarize important human studies investigating the use of PBT in spinal chordoma treatment.

Literature Review

Indelicato et al., reported their results of 51 patients with spinal chordomas or chondrosarcomas with either definitive or adjuvant PBT.[7] They found the 28 patients treated with PBT alone had a 54% 4-year local control rate, compared to 62% in the remaining 23 patients treated with a combination of PBT and photon-based radiotherapy.[7] The difference in 4-year local control rate between the two groups was not found to be statistically significant.7 Of note however, is that a large difference in the 4-year local control rate was reported between patients irradiated at disease onset (71%) compared to patients receiving radiotherapy only at disease recurrence (19%).[7] It is not clear from the study whether this observed difference represents the increased aggressiveness and resistance of recurrent tumours to radiotherapy or a true benefit of early institution of radiotherapy in this patient population.[7] Overall 4-year survival in this patient sample was 72%, with 86% of patients being free of metastatic disease at the 4-year time point.[7]

Stieb et al., conducted a review of 76 patients with spinal chordomas (n=55) or chondrosarcomas (n=21) who received PBT for disease management.[8] They did not stratify results based on tumour type, though the 5-year overall survival was reported to be 75%, 5-year local control rate was 61%, and disease free survival was 58%.[8]

Kabolizadeh et al., evaluated 40 spinal chordoma patients treated with definitive PBT without surgical resection and found local control rates at 3 and 5 years to be 96.9% and 85.4%, while overall disease-specific survival was 97.2% at 3 years and 89.4% at 5 years respectively.[9] In this study, tumour volume was found to be a significant prognostic indicator, with larger tumour volumes associated with reduced survival.[9]

Park et al., reported their findings of 27 spinal chordoma patients treated with some combination of surgery and proton, and photon therapy.10 Of the 21 patients treated with combined surgery and adjuvant radiation, 10-year local control was 90.9% in the primary chordoma patients, compared to 19.1% in the recurrent chordoma patients.[10] A 10-year disease-free survival was reported as 90.9% in the primary chordoma patients and 14.3% in recurrent chordoma patients. The 6 patients treated with radiation alone faired poorly, with 2 patients developing distant metastases and 2 developing local recurrence within 4 years of treatment.[10]

Banfield et al., published outcomes of 67 spinal chordoma patients treated with definitive PBT and found overall survival rates of 83.5% at 5 years and 65.9% at 8 years.[11] Disease-free survival was 64% at 5 years and 44.1% at 8 years.[11] Larger tumour volumes were associated with lower survival and local control frequencies though these differences were not found to be statistically significant.[11] Higher PBT doses were associated with lower probability of local recurrence with a *p*-value of 0.074.[11]

Walser et al., studied 60 sacral chordoma patients who received either definitive radiation or adjuvant radiotherapy.[12] Fifty of these patients had received isolated PBT and the remaining 10 had received a combination of proton and photon therapy. After 4 years, 20 of these patients were found to have disease progression, with 12 patients having isolated local progression and the 8 having combined local progression and metastatic disease.[12] On univariate analysis, the interval between surgery and PBT, PBT treatment for disease recurrence, and combination therapy of PBT with hyperthermia or photon-based therapy were not found to bear statistically significant influences on survival and local control frequencies.[12]

Aibe et al., reviewed 33 primary sacral chordoma patients who were prescribed definitive PBT.[13] At 3 years post-treatment, the local progression-free survival, distant metastasis-free survival, disease-free survival, cause-specific survival, and overall survival rates were 89.6%, 88.2%, 81.9%, 95.7%, and 92.7% respectively.[13] Six patients developed disease progression, of whom 3 had isolated local progression, 2 had local progression in conjunction with distant metastasis, and 1 had isolated distant metastasis. Sacral tumours limited to the S2 vertebra and below had a 100% local progression-free survival rate compared to 76.2% in those whose tumours extended above, and this difference was found to be statistically significant.[13]

Conclusion

PBT shows significant promise as a treatment modality for spinal chordomas. Outcomes seem to be better when PBT is used as an adjuvant measure to surgical resection than when it is used as definitive treatment.

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