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Radiotherapy for Solitary Bony or Extramedullary Plasmacytoma

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Abstract. *Background/Aim: This study aimed to determine the oncological outcomes associated with curative radiotherapy for solitary bony or extramedullary plasmacytomas by drawing on clinical data from a single tertiary center. This study aimed to provide a comprehensive understanding of the efficacy of radiotherapeutic interventions and delineate the patterns of disease recurrence. Patients and Methods: Eleven consecutive patients diagnosed with solitary bony or extramedullary plasmacytomas and treated between May 2007 and November 2023 were retrospectively screened. Different radiotherapy doses and fractionations were employed, and statistical analyses were performed to assess overall survival (OS) and disease-free survival (DFS). Results: Among the 11 patients (9 males and 2 females), primary tumors were located within the bone in seven patients, whereas extramedullary tumors were observed in four patients. The median prescribed radiation dose was 46 Gy. The 5-year OS and DFS were 83.3% and 28.9%, respectively. Progression to multiple myeloma occurred in four patients with primary bony plasmacytoma. Local control rate was 88.9%, and one patient experienced distant metastasis after 32 months. Bony plasmacytoma has a high tendency of leading to multiple myeloma rather than extramedullary plasmacytoma (5-year progression to multiple myeloma-free survival rate, 20.8% vs. 100%, p=0.08). Conclusion: Radiotherapy is effective for solitary plasmacytomas with favorable local control and high objective response rates. A comparison with the existing literature supports the role of radiotherapy in the management of these conditions. The differences in outcomes between bony and extramedullary plasmacytomas emphasize the need for personalized treatment approaches.*

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Plasma cells derived from B lymphocytes continuously produce antibodies that are critical for protecting against pathogens (1). The quantity and quality of these antibodies are correlated with vaccine efficacy, and the lifespan of plasma cells determines the duration of humoral immunity (2). Solitary plasmacytoma, a rare manifestation of plasma cell neoplasia, manifests as a clone of monoclonal plasma cells either within or outside the bone and is categorized as either solitary bone plasmacytoma or solitary extramedullary plasmacytoma (3, 4). Polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, and skin changes, defined as POEMS syndrome, is a paraneoplastic condition characterized by the occurrence of plasmacytoma (5).

Optimal management strategies for plasmacytomas remain an area of ongoing investigation (6). Radiation therapy is commonly used as a primary treatment modality for plasmacytoma (7). However, there is limited evidence supporting its efficacy, as comprehensive studies focusing on the oncological outcomes of curative radiotherapy are scarce. This study aimed to reveal the oncological outcomes associated with curative radiotherapy for solitary bony or extramedullary plasmacytomas using clinical data gathered from a single tertiary center. By examining a homogeneous cohort from a single tertiary center, we aimed to better understand the oncological outcomes of curative radiotherapy. Our investigation aimed to shed light on the efficacy of radiotherapeutic interventions and delineate the patterns of disease recurrence.

Patients and Methods

We retrospectively screened consecutive patients who were diagnosed with solitary bony or extramedullary plasmacytomas and treated at our institution between May 2007 and November 2023. In this retrospective study, we identified 13 patients with solitary plasmacytoma and excluded two patients for whom radiotherapy was conducted with palliative intent. Ultimately, 11 patients were included in the study. All patients had clinically confirmed plasmacytomas and received curative radiotherapy. 18F-fluorodeoxyglucose positron emission tomography with computed tomography (18F-FDG PET-CT) was used to evaluate solitary lesions without distant lesions.

Three-dimensional conformal radiotherapy (3D-CRT) and intensity-modulated radiation therapy (IMRT), which includes helical tomotherapy or volumetric modulated arc therapy (VMAT), were utilized in the administration of radiotherapy. Planned CT image data were reconstructed with a slice thickness of 5 mm for 3D-CRT and 2 mm for IMRT. The treatment plan for solitary body plasmacytoma of the thoracic vertebrae is shown in Figure 1. The dose and fractionation of radiotherapy were determined by a radiation oncologist at the time of treatment.

Statistical analyses were performed using the R statistical package (R Foundation for Statistical Computing, Vienna, Austria). Overall survival (OS) is defined as the time from the start of radiotherapy to death from any cause. Disease-free survival (DFS) is defined as the time from the start of radiotherapy to plasmacytoma recurrence, progression to multiple myeloma, or death. Survival curves were assessed using the Kaplan–Meier method, and statistical significance was defined as a p-value of <0.05.

Results

Among the 11 patients included in this study, the cohort consisted of nine males and two females. Table I summarizes the clinical data and treatment outcomes of the patients. The primary tumor was the bone in seven patients whereas in four patients tumors were extramedullary. The median prescribed dose was 46 Gy (range=40-50.4 Gy), with a median fractionation of 24 Gy (range=20-28 Gy). All but one patient was treated with radiotherapy alone, but one patient (Patient J) was treated with radiotherapy followed by planned surgery. An objective response was achieved in 10 patients, however one patient (Patient G) exhibited disease progression after radiotherapy. This patient was subsequently treated with systemic therapy, involving thalidomide and dexamethasone administration, followed by autologous peripheral blood stem cell transplantation.

The median follow-up time was 51.3 months (range=6.8-193.7 months). The actuarial 5-year OS and DFS for all patients were 83.3% [95% confidence interval (CI)=27.3-97.5%] and 28.9% (95%CI=4.6-60.5%), respectively. Four patients with primary bony plasmacytomas experienced progression to multiple myeloma (Patients A, C, E, and F). The actuarial 5-year progression to multiple myeloma free survival rate for all patients was 46.3% (95%CI=11.2-76.2%). The median time to multiple myeloma was 33.8 months (range=7.3-55.3 months). Bony plasmacytoma more frequently progressed to multiple myeloma than extramedullary plasmacytoma (5-year progression to multiple myeloma free survival rate, 20.8% *vs*. 100%, $p=0.08$) (Figure 2). Two patients experienced local failure, and the 5-year local control rate in this study was 88.9% (95%CI=43.3-98.4%). Distant metastasis the breast was found in one case (Patient H) 32 months after the initial radiotherapy.

Discussion

Our study aimed to evaluate the clinical outcomes of radiotherapy in patients with solitary bony or extramedullary plasmacytomas in a single-institution setting. Our results demonstrate the effectiveness of radiotherapy as a treatment modality for this relatively rare manifestation of plasma cell neoplasms. One of the findings of our study was that favorable local control was achieved with radiotherapy in the majority of cases. The high rate of local response observed in our cohort aligns with previous reports, emphasizing the efficacy of radiotherapy in achieving tumor control in plasmacytomas. This finding supports the notion that radiotherapy remains a cornerstone in the management of solitary bony or extramedullary plasmacytomas.

Ozsahin *et al*. analyzed 258 patients with solitary plasmacytomas without multiple myeloma, most of whom were treated with radiotherapy, with a median follow-up period of 56 months (8). They reported that patients with extramedullary solitary plasmacytoma exhibited higher OS (72% *vs*. 52%) and DFS rates (55% *vs*. 25%) than those with bone solitary plasmacytoma. The differences were statistically significant ($p<0.05$ for both). They also reported that the 5-year probability of developing multiple myeloma was 45%. In a retrospective study conducted by Knobel *et al*., in 206 patients with solitary plasmacytoma of the bone, the median follow-up was 54 months. The 5-year OS, DFS, and local control rates were 70%, 46%, and 88%, respectively (9). The International Lymphoma Radiation Oncology Group aims to standardize radiotherapy for solitary plasmacytomas (10). Suh *et al*. assessed the outcomes of radiotherapy in 38 patients with solitary plasmacytoma and demonstrated excellent local control, with a 10-year rate of 81%, a 10-year multiple myeloma-free survival was 54%, and OS was 35% (11). They also found that solitary bone plasmacytomas had a higher tendency to progress to multiple myeloma than the extramedullary type (10-year multiple myeloma free rate was 0% *vs*. 71%, $p=0.02$).

Currently, there is no definitive consensus on the optimal dose or fractionation of radiotherapy for patients with plasmacytoma. Elsayad *et al*. assessed the effectiveness of different radiotherapy parameters for solitary plasmacytoma in 84 patients treated between 2000 and 2019. They reported that a dose above 40 Gy correlated with a higher complete

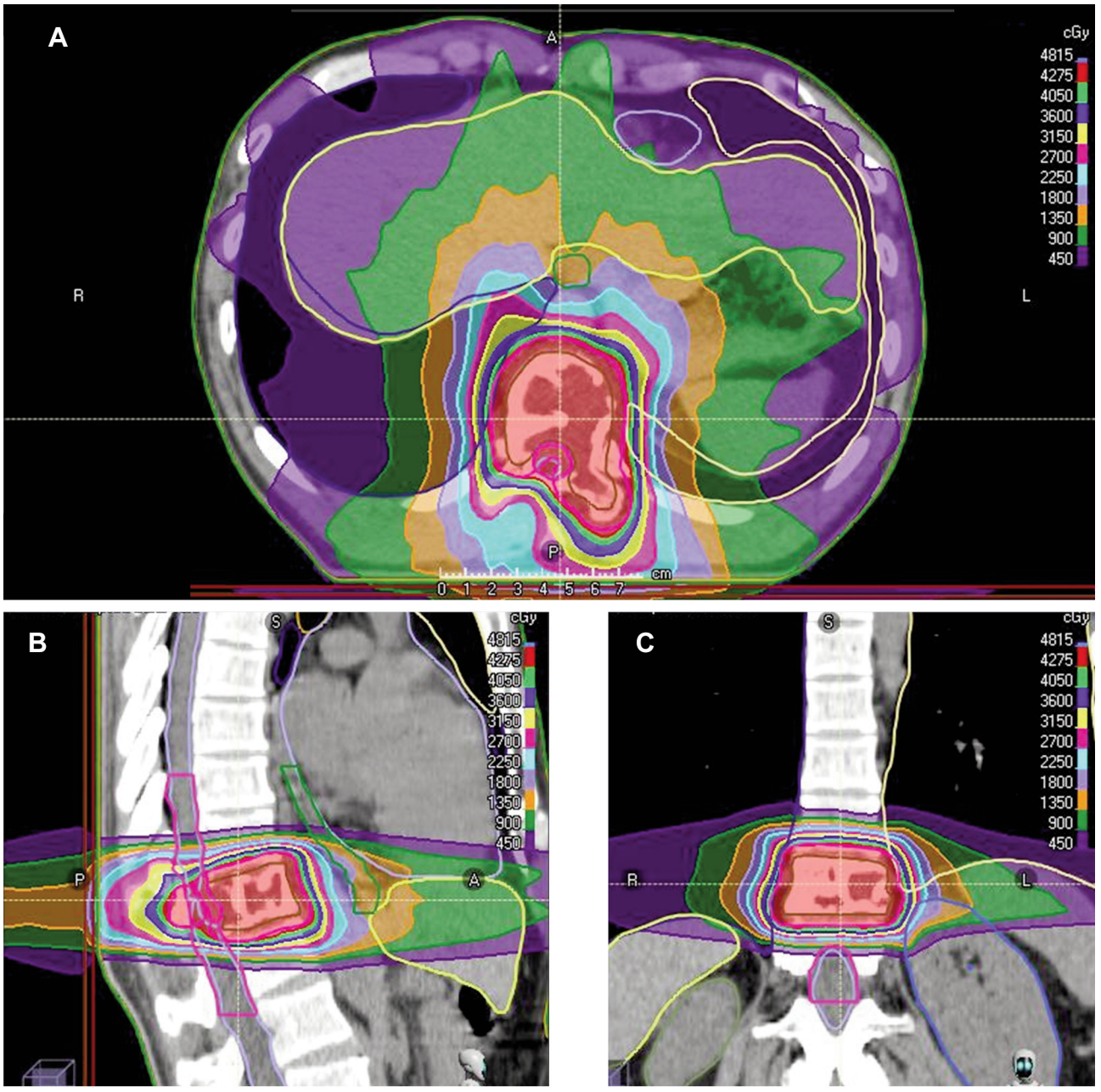

Figure 1. *The radiotherapy treatment plan utilized volumetric modulated arc therapy for bony plasmacytoma of the thoracic vertebra. Dose distribution in the transverse (A), sagittal (B), and coronal plane (C).*

remission and lower local relapse. Oertel *et al*. examined the efficacy of radiotherapy for solitary bone or soft tissue involvement in plasma cell neoplasia in 27 patients (12). They found a 76% local control rate, with better outcomes for primary lesions. High-dose radiotherapy (>45 Gy) showed an 87% overall response rate compared to 67% for low-dose radiotherapy (≤45 Gy), leading to longer survival. Their study suggested that radiotherapy was effective for extramedullary plasmacytomas, with potential benefits from dose escalation in specific patient subgroups.

Study limitations. It is retrospective and the sample size was relatively small. In addition, the variability in how patients were treated might have introduced bias. Larger prospective studies are required to confirm our findings and provide stronger evidence for making treatment decisions.

Table I. *Characteristics of 11 consecutive patients with plasmacytoma treated with definitive radiotherapy.*

Patient	Age	Sex	KPS	Type	Primary site	Dose and fraction	Outcome	Time to event (months)	Duration to last follow-up (months)	Status of last follow-up
A	64	Male	90	Bony	Thoracic vertebra (Th2)	46 Gy/23 Fr	Progression to MM	25.3	81.2	Alive
B	38	Male	90	Bony	Thoracic vertebra (Th4)	44 Gy/22 Fr	NED	-	152.2	Alive
C	58	Male	90	Bony	Thoracic vertebra (Th11)	50.4 Gy/28 Fr	Progression to MM	7.3	18.6	Alive
D	49	Male	90	Bony	Thoracic vertebra (Th11)	45 Gy/25 Fr	NED	-	6.8	Alive
E	78	Male	90	Bony	Rib	46 Gy/23 Fr	Progression to MM	55.3	58.8	Alive
F	60	Male	80	Bony	Mandible	48 Gy/24 Fr	Progression to MM	42.3	51.3	Dead
G	47	Male	90	Bony	Ilium	45 Gy/25 Fr	Local relapse	1.5	16.7	Alive
H	52	Female	90	Extramedullary	Nasal cavity	46 Gy/23 Fr	Distant relapse	32.1	112.4	Alive
I	93	Male	80	Extramedullary	Nasal cavity	50 Gy/25 Fr	NED	-	15.9	Alive
J	48	Male	90	Extramedullary	Occipital scalp	40 Gy/20 Fr	Local relapse	78.1	193.7	Alive
K	54	Female	70	Extramedullary	Frontal lobe	50 Gy/25 Fr	NED	-	35.5	Alive

KPS: Karnofsky Performance Status; MM: multiple myeloma; NED: no evidence of disease.

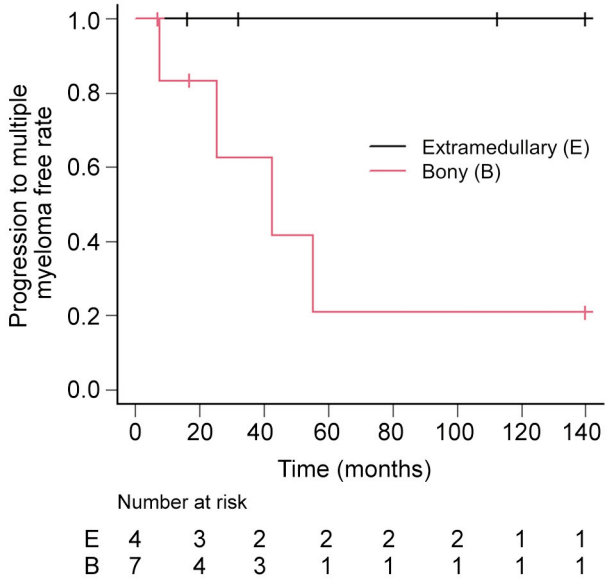

Figure 2. *Kaplan–Meier curve of the progression to multiple myeloma free survival rate stratified by bone and extramedullary plasmacytoma.*

Conclusion

Our experience shows that radiotherapy effectively controlled solitary bony or extramedullary plasmacytomas in a single hospital setting. Differences in outcomes between bony and extramedullary structures and between bony structures are important when considering treatment strategies.

Conflicts of Interest

The Department of Comprehensive Radiation Oncology, to which Masanari Minamitani and Shingo Ohira belong, is an endowment department, supported by an unrestricted grant from Elekta K. K. and Chiyoda Technol Corporation. However, no funding was received for conducting this study.

Authors' Contributions

All Authors contributed significantly to the conceptualization and design of the study, acquisition, interpretation, and validation of the data, drafting, critical revision of the manuscript, and final approval of the version to be published.

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