



Extramedullary Plasmacytoma of the Head and Neck: A Retrospective Study

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OBJECTIVE

Solitary extramedullary plasmacytomas (SEP) are rare plasma cell tumors that primarily occur in the head and neck regions. Due to their rarity, retrospective series can provide valuable insights into their clinical behavior and management, contributing to the refinement of treatment strategies. This study aimed to report cases of SEPs in the head and neck region treated with radiotherapy (RT) over the last 20 years.

METHODS

Ten patients were enrolled in this study between January 2004 and January 2024. Their clinicopathological features and treatment protocols were recorded, and disease outcomes were analyzed.

RESULTS

The most common tumor site was the nasopharynx (n=5), followed by the nasal cavity (n=2). Nine of ten patients were initially treated with RT at the primary site. The median RT dose was 45.5 Gy (40–58). Complete response (CR) was achieved in nine of 10 patients. The median survival duration was 74 months. The 5-year progression-free survival (PFS) rate was 85%. Only one patient developed a new bone plasmacytoma during the follow-up. No patient experienced transformation to multiple myeloma.

CONCLUSION

The prognosis of SEP is favorable, with rare recurrence, metastasis, and transformation to multiple myeloma. Further multicenter prospective studies are necessary to optimize management strategies for this rare entity.

Keywords: Extramedullary plasmacytoma; head and neck; nasal cavity; nasopharynx; solitary plasmacytoma.

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INTRODUCTION

Solitary plasmacytomas are a subset of plasma cell neoplasms, ranging from monoclonal gammopathy of undetermined significance to multiple myeloma (MM). [1] Histologically, they are characterized by increased proliferation of plasma cells. Unlike MM, solitary plasmacytomas do not exhibit end-organ damage or wide-

spread bone involvement. These tumors account for 5% of all plasma cell neoplasms and can be categorized as solitary extramedullary plasmacytomas (SEPs) or solitary bone plasmacytomas.[2] SEPs constitute one-third of all plasmacytoma cases.[3]

Extramedullary solitary plasmacytomas can develop throughout the body, with a predilection for the head and neck region.[3] These tumors typically reside sub-

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mucosally in the upper respiratory tract and often lead to symptoms such as obstruction, swelling, and bleeding.[4] The median age at SEP diagnosis is the 5th or 6th decade, approximately 10 years younger than that for MM diagnosis.[5,6] A notable sex disparity has been reported in SEP cases, with two-thirds of the patients being male.[7] Diagnostic evaluation involves a comprehensive approach including medical history taking, physical examination, blood tests, imaging studies, bone marrow biopsy, serum protein electrophoresis, urine evaluation for myeloma proteins, and skeletal survey.[1]

The rarity of SEPs has resulted in a paucity of high-level evidence regarding their treatment. Given the radiosensitivity of these tumors, radical RT is typically administered after biopsy.[8] RT doses reported in case reports from the 1950s to the present vary widely, ranging from 35 to 65 Gy.[8–10] Local control rates following RT have been reported to range from 80% to 100%.[8–15] The benefits of elective lymphatic irradiation remain unclear, and it is generally not recommended.[7]

Surgical intervention is not initially advised because of the challenges associated with achieving complete tumor removal and the potential for morbidity in the head and neck region.[8,16] Adjuvant RT is often necessary even when surgical excision is performed. Some case studies have suggested that combined treatment modalities may result in improved local control.[7] The role of systemic therapy at the plasmacytoma stage remains unclear, and it is not routinely recommended.[2]

RT achieves high local control rates during the treatment of plasmacytomas. However, posttreatment disease progression can manifest as local recurrence, new plasmacytoma sites (most commonly in the bone), or transformation to MM. Transformation to MM is less frequent in patients with extramedullary plasmacytomas than in those with bone plasmacytomas.[7] Progression to MM is a significant prognostic factor for survival. Various factors, such as tumor size, bone involvement, and radiation dose, have been investigated for their predictive value.[3,5,7,13] Nonetheless, the very low incidence of this tumor type precludes the optimal determination of predictive factors without prospective studies.

Given the rarity of SEPs, insights from retrospective studies are essential for bridging existing knowledge gaps, refining treatment protocols, and providing a foundation for future research to improve patient care and prognosis. Understanding the clinical behavior of these tumors, particularly in the head and neck region, is crucial for tailoring effective and individualized treatment strategies. This study aims to evaluate the clinical features and treatment man-

agement of SEPs in the head and neck region reported over the last 20 years at Istanbul University Oncology Institute and Koç University.

MATERIALS AND METHODS

The medical records of all patients treated for SEPs of the head and neck at the two institutions between January 2004 and January 2024 were retrospectively reviewed. The Istanbul University Oncology Institute Review Board approved this study (Date: 29/04/2025, No: 2025/1174) and the study is conducted according to Declaration of Helsinki. Patient demographic data, initial tumor presentation, treatment details and survival outcomes were retrieved from institutional databases. Written informed consent was obtained from the all patients.

The inclusion criteria were as follows:[17]

1. Histologically confirmed plasmacytoma of the soft tissue of the head and neck region,
2. Normal skeletal survey,
3. Normal bone marrow biopsy,
4. No evidence of end-organ damage (anemia, hypercalcemia, renal insufficiency).

Patients with solitary bone lesions were excluded. Ten patients from two institutions were analyzed.

Systemic staging for all patients included physical examination, complete blood counts, biochemical analysis, serum and urine protein electrophoresis, and bone marrow aspiration/biopsy. Regarding imaging modalities, while positron emission tomography (PET-CT) has been performed systematically for initial staging and follow-up since its clinical introduction in our center in 2009, staging for patients treated prior to this period relied on conventional methods, including skeletal surveys (plain radiography) and/or magnetic resonance imaging (MRI) or computed tomography (CT).

Response assessment was typically performed 3 to 6 months after the completion of therapy, preferably utilizing MRI and/or PET-CT scans. Treatment response was assessed using the RECIST (Response Evaluation Criteria in Solid Tumors) criteria v1.1, where CR was defined as the disappearance of all target lesions on follow-up imaging.

Following the completion of RT, patients were followed concurrently by radiation oncology and hematology clinics every 3 months for the first 2 years, every 6 months for the subsequent 3 years, and annually thereafter. Follow-up evaluations consisted of physical and endoscopic examinations, laboratory tests (including complete blood count, biochemistry, and serum

Table 1 Clinical characteristics of patients with solitary extramedullary plasmacytomas

Patient	Age	Sex	Tumor location	Tumor diameter (cm)	Bone erosion	Immunohistochemical analysis	First surgery	PET-CT	Bone marrow biopsy
1	37	M	Maxillary sinus	3.1	No	Plasma cell infiltration	Right maxillectomy	No	Normocellular
2	63	M	Nasopharynx	2	No	Lambda type	Biopsy	Yes	Normocellular
3	68	M	Nasopharynx	2.3	No	Lambda type	Biopsy	No	3–5% plasma cells
4	57	M	Nasopharynx	2.3	No	Kappa type	Excisional biopsy	Yes	<5% plasma cells
5	51	M	Larynx	1	No	Lambda type	Biopsy	Yes	<5% plasma cells
6	49	M	Nasopharynx	2.2	No	Kappa type	Biopsy	Yes	3–5% plasma cells
7	83	M	Nasal cavity	6.5	Yes	Lambda type	Biopsy	Yes	3% plasma cells
8	44	M	Gingiva	2.7	Yes	Plasma cell infiltration	Biopsy	Yes	3–5% plasma cells
9	66	M	Nasopharynx	2.3	No	Kappa type	Biopsy	Yes	Normocellular
10	70	F	Nasal cavity	2.2	No	Kappa type	Biopsy	Yes	Normocellular

M: Male; F: Female; PET-CT: Positron emission tomography.

protein electrophoresis), and imaging (CT or MRI of the head and neck). PET-CT was performed in cases of clinical or radiological suspicion to assess local control or potential systemic progression.

Statistical Analysis

The data were analyzed, and categorical variables were summarized by frequency and percentage, and quantitative variables, by median and range. Statistical analyses were performed using IBM SPSS, version 26.0, program. Progression-free survival was calculated from the date of diagnosis to any type of disease progression. Overall survival was calculated from the date of diagnosis to death or the last follow-up date. Survival curves were plotted using the Kaplan–Meier method.

RESULTS

Ten patients were diagnosed with SEPs in the head and neck region, nine of whom were male. The median patient age was 60 (range: 37–83). Detailed clinicopathologic data are presented in Table 1.

The majority of cases (80%) were localized in the sinonasal area, with the nasopharynx being the most frequent site. Immunohistochemistry showed an equal distribution of kappa and lambda light-chain predominance. Systemic involvement was ruled out in all patients; PET-CT scans performed in eight patients (80%) showed no distant metastasis. Bone marrow biopsies confirmed less than 5% plasma cell infiltration in all cases.

Diagnostic biopsy was the primary surgical intervention in eight patients, while two cases required

more extensive procedures: one excisional biopsy for a nasopharyngeal tumor and one maxillectomy for a maxillary sinus tumor. All 10 patients received RT as the definitive treatment, with a median dose of 45.5 Gy (range: 40–58 Gy). The majority (n=7) were treated with intensity-modulated radiation therapy (IMRT), and one patient received elective neck irradiation.

Regarding clinical outcomes, nine patients (90%) achieved CR. One patient exhibited minimal residual disease on PET-CT and MRI three months post-RT; however, the lesion remained stable during 16 months of radiological follow-up (Table 2).

The median survival time was 74 months (range: 13–187 months), with a 5-year PFS rate of 85% (Fig. 1). During the follow-up period, only one patient developed a solitary bone plasmacytoma, and treated with systemic treatment. None of the patient's condition progressed to MM.

DISCUSSION

Most plasma cell neoplasms are MM, with solitary plasmacytomas accounting for approximately 5–6% of all plasma cell neoplasms.[2] Of the solitary plasmacytomas, approximately 20–30% are extramedullary and often occur in the head and neck region.[3,18] Over the past 20 years, Istanbul University Oncology Institute and Koç University treated 10 patients with extramedullary plasmacytomas in the head and neck region. In our cohort, nine of ten patients achieved CR, with an overall survival of 100% and a five-year PFS rate of 85% at the last follow-up.

Table 2 Treatment characteristics of patients with solitary extramedullary plasmacytomas

Parameter	Subgroup	n	PR (n)	New lesion (n)	MM (n)
Tumor size	≤5 cm	9	0	1	0
	>5 cm	1	1	0	0
Bone erosion	Absent	8	0	1	0
	Present	2	1	0	0
Anatomic Site	Sinonasal	8	1	1	0
	Others	2	0	0	0
RT Dose	40–45 Gy	5	0	0	0
	>45 Gy	5	1	1	0
Treatment modality	Definitive RT	8	1	1	0
	Surgery + RT	2	0	0	0
RT technique	IMRT	7	1	1	0
	2DRT	3	0	0	0

RT: Radiotherapy; Gy: Gray; MM: Multiple myeloma; 2DRT: Two-dimensional radiotherapy; IMRT: Intensity-modulated radiotherapy; PR: Partial response.

Extramedullary plasmacytomas tend to recur locally, and progression to MM is less common in this patient group than in patients with bone plasmacytomas, affecting 10–30% of the patients over a decade.[2] Nevertheless, owing to the risk of progression to MM, these patients require ongoing hematological monitoring. Progression from a plasmacytoma to MM can take years, making long-term follow-up crucial for understanding the prognosis. In our cohort, none of the patients experienced local recurrence or progression to MM, despite 60% of our sample having a follow-up period exceeding five years. Although one patient developed a new solitary bone plasmacytoma, this was successfully managed with salvage therapy.

In a meta-analysis of 315 patients, the most common site of involvement was the sinonasal region (paranasal sinuses, 22.3%; nasal cavity, 17.5%; nasopharynx, 10.8%).[7] Furthermore, the Surveillance, Epidemiology, and End Results (SEER) analysis of 690 patients found that nasal cavity and paranasal sinus involvement accounted for 32.3% of the cases, while nasopharyngeal involvement was not reported separately. [19] In our study, eight of the 10 patients had tumors located in the sinonasal region.

For patients with SEPs, the presence of bone erosion and a tumor diameter exceeding five cm are associated with worse survival and an increased risk of progression to MM.[7,13] Large tumors, especially those involving the sinonasal region, present significant surgical challenges and are often managed primarily with RT. One patient in our cohort with a bulky tumor and extensive nasal cavity bone invasion exhibited residual anatomic and metabolic findings at the

initial post-RT evaluation. Despite these features, the lesion has remained stable over 16 months of follow-up without additional intervention. Similarly, another patient with mandibular bone destruction achieved a CR despite minimal post-treatment FDG uptake and persistent minor bone erosion on imaging. These cases indicate that in highly radiosensitive tumors like SEP, post-treatment imaging findings even in the presence of initial bone destruction must be interpreted with caution to avoid unnecessary over-treatment.

For the treatment of SEPs in the head and neck region, RT is typically administered as the primary treat-

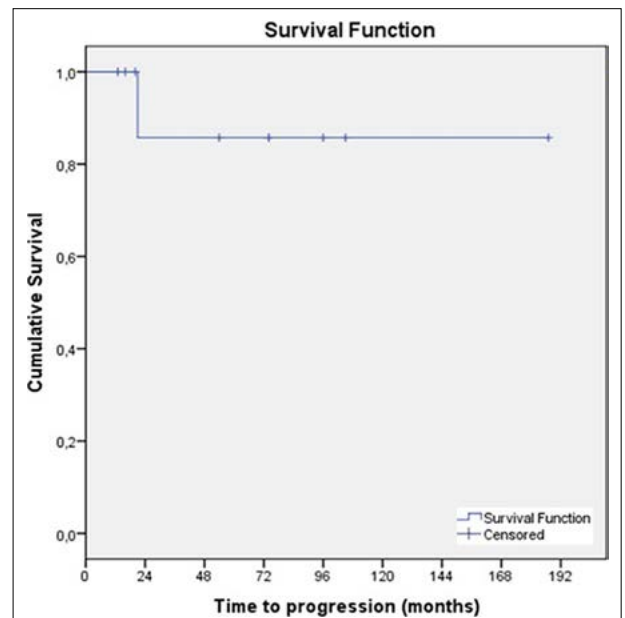


Fig. 1. Progression-free survival curve of 10 patients.

ment option, with a local control rate of up to 80%. [8–15] Owing to the high risk of morbidity and radio-sensitivity, surgery is generally not the preferred primary treatment option. Achieving clear surgical margins is challenging, and RT is often administered in addition to surgery. Some studies have reported higher local control rates when surgery and RT are combined.[7] In our series, the majority of patients (n=8) were treated with definitive RT alone, and none experienced local recurrence or progression. A recent meta-analysis by Vasudevan et al.[20] examined 742 patients with SEPs in 12 studies, including those with tumors outside the head and neck region. They found that patients who received RT had significantly lower rates of progression to MM than those treated with surgery alone. The authors attributed this finding to the ability of RT to provide sufficient coverage of microscopic residual tumor cells, which may be missed during surgical excision. Within the limitations of our small cohort, these outcomes are consistent with the view that RT can be effective as a standalone treatment for SEPs in the head and neck region.

In various studies, the radiation dose administered for treating head and neck SEPs ranges from 30 to 65 Gy.[8–10] Evidence suggests that doses exceeding 40 Gy or 45 Gy improve local control.[7,10,21] The International Lymphoma Radiation Oncology Group (ILROG) guidelines recommend a radical treatment dose of 40–50 Gy for head and neck SEPs.[2] Nevertheless, establishing RT dosing guidelines remains challenging owing to the limited number of prospective studies, and the correlation between the RT dose and PFS warrants further investigation. In our series, the median radiation dose was 45.5 Gy and radiation doses ranged from 40 to 58 Gy. Even at the minimum dose of 40 Gy, all patients (n=3) achieved a CR and maintained long-term local control. The use of higher doses (up to 58 Gy) in some cases reflected individualized treatment decisions from the earlier years of the study.

SEPs are generally localized diseases, with neck metastasis occurring in 5–20% of the cases.[7] Advances in radiological imaging technologies have facilitated the detection of neck metastases. During follow-up, neck recurrence is observed in approximately 5% of patients, and salvage treatments demonstrate a high success rate. Therefore, elective lymphatic irradiation during RT is controversial and its benefit is unclear if neck metastasis is not detected.[7] According to ILROG guidelines, elective lymphatic irradiation is not recommended unless there is a high risk of metastasis, as observed in patients with bulky tumors.[2] In our series, elective neck treatment was administered to only one patient.

Our study covers a 20-year period, which inherently introduces some heterogeneity due to advancements in RT techniques and imaging modalities. The transition from 2D-RT to modern techniques like IMRT represents a significant shift in treatment precision. Despite these technological differences, the consistently high local control rates were observed across our cohort. The outcomes observed in our study, although based on a limited number of patients, are broadly consistent with the reported literature on head and neck SEPs. However, due to the inherent limitations of a small, retrospective cohort, our results should be interpreted with caution and validated by larger, multicenter pooled analyses.

Limitations of the Study

This is a retrospective study with a small number of patients. Since patients were collected over a long period of 20 years, there is variability in the RT techniques, radiation fields and doses administered. In rare tumors like SEP, where treatment approaches are based on retrospective data, there can be significant differences in approach even among physicians in the same clinic.

CONCLUSION

This study indicates that RT provides high local control and a favorable prognosis for SEPs of the head and neck. Although no progression to MM was observed within this cohort, the potential for late systemic transformation warrants long-term multidisciplinary monitoring. Given the rarity of the disease and the limited sample size, these findings should be interpreted as exploratory, underscoring the need for larger multicenter studies to further optimize management strategies.

Ethics Committee Approval: The study was approved by the Istanbul University Ethics Committee (no: 2025/1174, date: 29/04/2025).

Informed Consent: Written informed consent was obtained from all patients.

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