Clinical and prognostic features of plasmacytomas: A multicenter study of Turkish Oncology Group-Sarcoma Working Party

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To identify the outcomes of prognostic factors of solitary plasmacytoma mainly treated with local radiotherapy (RT). The data were collected from 80 patients with solitary plasmacytoma (SP). Forty patients (50.0%) received radiotherapy (RT) alone while 38 of them (47.5%) were treated with surgery (S) and RT. The median radiation dose was 46 Gy (range 30–64). The median follow up was 2.41 years (range 0.33–12.33). Ten-year overall survival (OS) and local relapse-free survival (LRFS) were 73% and 94%, respectively. The median progression-free survival (PFS) and multiple myeloma-free survival (MMFS) were 3.5 years and 4.8 years, respectively. On multivariate analyses, the favorable factors were radiotherapy dose of ≥50 Gy and RT + S for PFS and younger age for MMFS. For the patients with medullary plasmacytoma, the favorable factor was younger age for MMFS. RT at ≥50 Gy and RT + S may be favorable prognostic factors on PFS. Younger patients, especially with head-neck lesion and without pre-RT macroscopic tumor, seem to have the best outcome when treated with RT ± S. Progression to MM remains as the main problem especially for older patients. Am. J. Hematol. 83:702–707, 2008. © 2008 Wiley-Liss, Inc.

Introduction

Solitary plasmacytoma (SP) is a rare presentation of plasma cell neoplasm and accounts for 5–10% of all plasma cell neoplasm in the literature [1–4]. It is characterized by a localized collection of malignant plasma cells without evidence of a systemic plasma cell proliferative disorder. Solitary plasmacytomas are classified as plasmacytoma of the skeletal system and soft tissue (extramedullary) plasmacytoma [5].

Both represent different groups of neoplasm in terms of location, tumor progression, and overall survival rate [6,7]; however, they share many of the biologic features of other plasma cell disorders [2,8]. Solitary plasmacytomas of bone (SPB) usually occur in the vertebra and skull and are more common than solitary extramedullary plasmacytomas (SEP) [9]. SEP mostly arises in the head and neck [5,10–14]. The median age of patients with either SPB or SEP is 55 years [1]. SP has a male-to-female ratio of 2:1 [5,10,11,15,16].

Local radiotherapy (RT) is a treatment of choice [1,2,12,16]. The optimal treatment is moderate-dose RT and occasionally surgery (S) giving adequate local control [5,15,17–23]. Adjuvant chemotherapy does not improve survival. Patients with SEP have a relatively low risk of progressing to multiple myeloma (MM) and have improved survival compared with those presenting with SPB which develops into MM in 50–60% of patients [1,15,19,24]. Despite local radiation with curative intent, the median time to progression to MM is 2–3 years [20,25–28].

There are no conclusive data in the literature on the optimal RT dose for SP. A wide range of doses varying from 30 to 70 Gy were reported by many researchers [2,9,13, 17,20,21,26,27]. The reported optimal dose used for local control is 35–50 Gy (depending on the size or the site of tumor) [10,15–17].

We have reviewed the results of a retrospective multicenter study of a large cohort of patients with SP from the centers in Turkey. In this study, we attempt to identify factors that predict for overall survival (OS), progression-free survival (PFS), MM-free survival (MMFS), and local relapse-free survival (LRFS).

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Materials and Methods

Between 1991 and 2007, 116 patients consecutively treated with curative intent for a SP without evidence of MM formed the population of this retrospective multicenter study of Turkish Oncology Group (TOG) - Sarcoma Working Party. Thirty-six patients were considered to be lost to follow-up and 80 patients, who had a regular follow-up of a minimum of 3 months after the diagnosis and who were confirmed to meet the following eligibility criteria for being included in the study by the participating centers, were included in the analysis. The medical records of the patients were analyzed for their demographic details, tumor description, management and outcome. One "hematologist" and two radiation oncologists reviewed the data. In all cases, it was confirmed that appropriate investigations (bone marrow biopsy, urine and plasma electrophoresis, and skeletal diagnostic workup) had been carried out to exclude a diagnosis of MM. In the study, the patients were diag-

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Conflict of Interest: Nothing to report.

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nosed as SP when they met the following criteria: (1) a biopsy proven plasma cell tumor involving a single extramedullary or medullary site, (2) a bone marrow biopsy showing less than 10% plasma cells without evidence of clonality, (3) no additional pathologic lesions in the skeletal diagnostic workup (imaging with X-ray skeletal survey and/or tomography and/or magnetic resonance), (4) absence of anemia, hypercalcaemia, or renal impairment attributable to myeloma, (5) low concentrations of serum or urine monoclonal protein, if present [1,11,12].

Treatment

The type of treatment is demonstrated in Table I. Data about surgical treatment type were obtained in 36 of 38 patients treated with surgery (complete excision in 20 patients). Out of 20 patients treated with surgery with complete excision, 13 were SEP.

RT was directed to the radiological visible gross tumor volume with a sufficient margin. The data of regional lymph node irradiation were recorded in 21 patients with SEP (91.3% of the patients with SEP) and it was detected that nodes were included in 8 (38%) patients.

Radiation doses of 30–64 Gy in 10–32 fractions were delivered with 1.8–3 Gy fractions (median 2 Gy) using megavoltage photons from a linear accelerator or Co60 gamma rays. To facilitate the comparison of different fractionation schedules used by different centers, the 2-Gy per fraction biologically effective dose (BED) was calculated according to the linear quadratic model: BED = nd (1+ [$d \div \alpha/\beta$]); where $\alpha/\beta = 10$ for tumor; n = number of fractions; d = dose per fraction [29]. Median dose was 46 Gy (range: 32.5–64.0), 46 Gy (range: 32.5–59.4), and 50 Gy (range: 32.5–64.0) in the whole group, SPB subgroup, and SEP subgroup, respectively.

The response to treatment was defined as complete, partial, or none according to Response Evaluation Criteria in Solid Tumors (RECIST) criteria [30]. Local failure was defined by no disappearance of soft tissue plasmacytoma and an increase in size or number of the lytic bone lesions.

Statistical methods

Time to any event was measured from the date of histological diagnosis. PFS and OS times were calculated to the nearest month, taken from the time of diagnosis to the time of first relapse or local progression and/or progression to MM (for PFS) or death/last recorded. For the LRFS rate, the event consisted of local failure, censoring patients without local relapse. For progression to MM, all patients without MM progression were censored.

Univariate analysis and multivariate analysis were applied separately for the whole group of 80 patients and for SEP and SPB groups. Actuarial survival analysis was performed according to the method described by Kaplan and Meier and the differences between groups were assessed using the log rank test [31,32]. P values <0.05 were considered to indicate statistical significance. The Cox stepwise regression analysis was employed to confirm significance of risk factors [33]. In multivariate analysis, we used eliminated variables stepwise (backward) by a significance of less than 10%. The data were analyzed with the SPSS 11.5 statistical package.

Results

The median age was 54 years (range: 16–76) and the male-to-female ratio was 1.22 (Table I). Pathological diagnosis was obtained in 80 patients. Surgical treatment was achieved with partial resection in 16 patients, and with complete resection in 20 patients (there was not any information about the type of surgery in 2 patients). Spinal column was the most frequent tumor site in patients with SPB (22 out of 57 patients) (Table II). Head and neck was the most frequent tumor site in patients with SEP (18 out of 23 patients).

Pre-RT macroscopic tumor information was recorded in 78 patients (97.5%), and among them, 57 (71.2%) had macroscopic tumor before RT. The largest diameter of the lesion was recorded accurately by using radiological images and/or pathological records in 55 patients (68.8%), and its median value was 5.0 cm (range: 0.5–20.0 cm). It was 5 cm or more in 28 patients (35.0%) and less than 5 cm in 27 patients (33.7%) (Table II). Tables I and II summarize the patient, disease, and treatment characteristics, respectively.

When the SEP and SPB subgroups were evaluated, SEP patients were younger (median ages are 47 and 54,

TABLE I. Characteristics of 80 Patients with Plasmacytoma

	All patients $n = 80$ (%)	SBP n (%)	SEP n (%)
Type of plasmacytoma		57 (71,3)	23 (28,7)
Age (median)	54 (16–76)	54 (16–76)	47 (20–76)
Gender			
Female	36 (45.0)	27 (47.0)	9 (39.1)
Male	44 (55.0)	30 (52.6)	14 (60.9)
Median fallow up time (year) $n = 80$	2.41 (0.33–12.33)	2.16 (0.33–12.33)	2.58 (0.33–8.21)
Largest tumor dimension at diagnosis			
<5 cm	27 (33.7)	17 (29.8)	10 (43.5)
≥5 cm	28 (35.0)	20 (35.1)	8 (34.8)
NA	25 (31.3)	20 (35.1)	5 (21.7)
Soft tissue component			
Yes	35 (43.7)	35 (61.4)	
No	21 (26.3)	21 (36.8)	
NA	24 (30.0)	1 (1.8)	
Pathologic fracture			
Yes	20 (25.0)	20 (35.1)	
No	47 (58.7)	36 (63.1)	
NA	13 (16.3)	1 (1.8)	
Pre-RT macroscopic tumor			
Yes	57 (71.2)	47 (82.5)	10 (43.5)
No	21 (26,3)	8 (14.0)	13 (56.5)
NA	2 (2.5)	2 (3.5)	0 (0.0)
Type of treatment			
Radiotherapy	40 (50.0)	30 (52.6)	10 (43.5)
Surgery + radiotherapy	38 (47.5)	26 (45.6)	12 (52.2)
NA	2 (2.5)	1 (1.8)	1 (4.3)
2 Gy/fr equivalent radiotherapy dose (Gy)			
≥50	30 (37.5)	17 (29.8)	13 (56.5)
≥40 and <50	42 (52.5)	33 (57.9)	9 (39.1)
<40 and ≥30	6 (7.5)	6 (10.5)	0 (0.0)
NA	2 (2.5)	1 (1.8)	1 (4.3)

SBP, solitary bone plasmacytoma; SEP, solitary extramedulary plasmacytoma; RT, radiotherapy; NA, not available.

TABLE II. Sites of Localization in the Patients With Extramedullary or Bone Plasmacytoma

Anatomic site	n (%)
Solitary plasmacytoma of bone	57 (71.3)
Vertebrae	22 (38.7)
Pelvis	8 (14.0)
Upper extremities	4 (7.0)
Lower extremities	4 (7.0)
Maxillary, mandibulary, and other facial bones	8 (14.0)
Skull	4 (7.0)
Other	7 (12.3)
	57 (100)
Solitary extramedullary plasmacytoma	23 (28.8)
Nasal cavity	3 (13.0)
Nasopharynx	3 (13.0)
Oral cavity	4 (17.4)
Other head&neck	8[a] (34.8)
Brain	1 (4.3)
Pelvis	1 (4.3)
Other	3 (13.0)
	23 (100)

[a] Two larynx, four cervical lymph nodes, one tongue, one parotid gland.

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TABLE III. Univariate Analysis (Logrank test) of Prognostic Factors in the Patients With Solitary Plasmacytoma

	N	10-year OS (%)	Log Rank *P*-value	Median PFS time (year)	Log rank *P*-value	10-year LRFS (%)	Log rank *P*-value	Median MMFS time year	Log rank *P*-value
All patients	80	(73)		3.5		(94)		4.8	
Age									
<55 year	37	(88)	0.3819	4.6	0.0960	(91)	0.2475	7.7	**0.0276**
≥55 year	32	(63)		2.9		(96)		3.2	
Gender									
Female	36	(66)	0.3384	3.3	0.6395	(94)	0.8692	7.4	0.7511
Male	44	(88)		4.1		(94)		4.4	
Type of plasmacytoma									
Bone	57	(68)	0.4783	3.2	0.0845	(94)	0.8199	4.1	0.1228
Extra medullary	23	(89)		7.4		(95)		7.4	
Site of plasmacytoma									
Head & neck	30	(83)	0.6213	7.4	**0.0246**	(96)	0.9234	7.7	0.0807
Other	50	(63)		3.1		(93)		4.1	
Largest tumor dimension at diagnosis									
<5 cm	27	(85)	0.8214	4.6	0.3967	(88)	0,3416	(51)[b]	0.0800
≥5 cm	28	7.6 year[a]		3.2		(96)		3.2	
Type of treatment									
RT	40	(58)	0.7025	2.6	**0.0359**	(94)	0.6256	3.2	**0.0222**
S + RT	38	(82)		7.4		(94)		7.7	
Pre-RT macroscopic tumor									
Yes	57	(69)	0.5689	3.1	**0.0214**	(94)	0.7476	4.1	**0.0369**
No	21	(89)		11.2		(95)		(56)[b]	
2 Gy/fr equivalent RT dose (Gy)									
≥50	30	(89)	0.2078	7.7	**0.0299**	(90)	0.0998	7.7	0.1084
<50	48	7.6 year[a]		2.7		(90)		3.2	

OS, overall survival; PFS, progression-free survival; LRFS, local relapse-free survival; MMFS, multiple myeloma-free survival; S, surgery; RT, radiotherapy.
[a] Median (year).
[b] 10-years MMFS rate (%).

respectively), more likely to be male (60.9% vs. 52.6%, respectively) and had smaller tumors prior to radiotherapy (presence of pre-RT macroscopic tumor is 42.5% vs. 82.5%, respectively). SEP patients had surgical operations and were treated with RT (52.2% vs. 45.6%, respectively) at a greater rate and they seemed to receive more than 50 Gy as RT dose at a higher rate (56.5% vs. 29.8%, respectively). Furthermore, SEP was located frequently (82.7%) in head and neck. SPB of 38.7% were located in the vertebra (Tables I and II).

Overall survival and progression-free survival

The median follow up was 2.41 years (range 0.33–12.33) for these patients. At analysis, 74 patients were alive (37 of them had progressed) and six had died. One patient was lost to follow-up when LR or MM was not present. Of the deceased patients, five had progressed to MM and this was their cause of death. One of them also had local recurrence. Five of the deceased patients were from SPB group whereas one of them was from SEP group. Of 37 patients who had been observed to progress, 24 had MM, four had local recurrence, one had both MM and local recurrence and eight had disease on another site. Of 37 progressed patients, 25 were in SBP group (21 progressed to MM, four had local recurrence).

The 10-year probability of OS was 73% in all patients, 68% in 57 patients with SPB, and 89% in 23 patients with SEP, respectively (Tables III and IV). The corresponding median PFS values were 3.5 years (95% CI: 2.25–4.81), 3.2 years (95% CI: 1.99–4.37), and 7.4 years (95% CI: 0.57–14.33), respectively (Table IV).

On univariate analyses, there was no significant prognostic factor influencing OS. The four factors that predicted for better PFS on univariate analysis were head-neck tumor site ($P = 0.0246$), absence of macroscopic tumor before radiation was instituted ($P = 0.0214$), the combination of surgery and radiation therapy ($P = 0.0359$), and RT dose of ≥50 Gy ($P = 0.0299$); however, on multivariate analysis, only the radiation therapy without surgery and lower radiation doses were significantly associated with lower PFS (Tables III and IV; Figs. 1 and 2). The respective hazard ratios (HR) were 2.197 ($P = 0.035$, 95% CI: 1.021–5.091) for RT alone and 2.279 ($P = 0.044$, 95% CI: 1.021–5.091) for RT dose of <50 Gy.

In the subgroup with SPB, the only factor that predicted for better PFS on univariate analysis was the combination of surgery and radiation therapy ($P = 0.0259$) (Table IV).

Myeloma-free survival

The median time for development of MM was 1.6 years (range: 0.28–12.03). Of all patients, 25 developed MM (21 of them were in SBP group). The median MMFS values were 4.8 years (%95 CI 1.46–8.24), 4.09 years (%95 CI: 2.41–5.77), and 7.45 years (%95 CI: 0.00–14.98) for SP group, SBP, and SEP subgroups, respectively (Table IV).

The three factors that predicted for better MMFS on univariate analysis were younger age (<55 years) ($P = 0.0276$), absence of macroscopic tumor before RT was instituted ($P = 0.0369$), and the combination of surgery and RT ($P = 0.0222$) (Table III, Fig. 3); however, on multivariate analysis, only the younger age was significantly associated with higher MMFS. The respective hazard ratio was 0.295 ($P = 0.027$, 95% CI: 0.100–0.871).

Concerning the patients with SPB, the two factors that predicted for better PFS on univariate analysis were younger age ($P = 0.0276$) and the combination of surgery and RT ($P = 0.0369$); however, on multivariate analysis,

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TABLE IV. Univariate Analysis (Logrank Test) of Prognostic Factors in the Patients With Bone Plasmacytoma

	N	10-year OS (%)	Log rank *P*-value	Median PFS time (year)	Log rank *P*-value	10-year LRFS (%)	Log rank *P*-value	Median MMFS time (year)	Log rank *P*-value
All patients	57	(68)		3.2		(94)		4.1	
Age									
<55 year	28	(90)	0.2406	3.3	0.2121	(92)	0.4058	4.8	**0.0485**
≥55 year	24	(53)		2.2		(95)		2.9	
Gender									
Female	27	(58)	0.2302	3.1	0.6333	(92)	0.5046	4.8	0.6886
Male	30	(89)		3.2		(95)		4.1	
Site of plasmacytoma									
Vertebra	35	(68)	0.9738	3.1	0.8461	(88)	0.2597	4.8	0.3494
Other	22	(78)		3.3		(97)		3.1	
Soft tissue component									
Yes	35	(77)	0.9699	3.5	0.1905	(93)	0.9621	4.8	0.1218
No	21	(69)		2.2		(94)		2.2	
Largest tumor dimension at diagnosis									
<5 cm	17	(91)	0.4855	4.6	0.2354	(87)	0.5345	4.8	0.0611
≥5 cm	20	7.6 year[a]		2.2		(95)		2.2	
Pathologic fracture									
Yes	20	(79)	0.4475	3.3	0.3553	(88)	0.6563	(72)[b]	0.0576
No	36	(72)		2.3		(97)		2.9	
Type of treatment									
RT	30	(52)	0.3730	2.1	**0.0259**	(91)	0.9348	2.9	**0.0176**
S + RT	26	(83)		4.6		(96)		7.7	
Pre-RT macroscopic tumor									
Yes	47	(66)	0.3098	2.9	0.0574	(92)	0.9874	3.2	0.0920
No	8	(100)		11.2		(100)		(83)[b]	
2Gy/fr equivalent RT dose (Gy)									
≥50	17	(81)	0.5458	4.6	0.1250	(100)	0.2212	4.8	0.3196
<50	39	7.6 year[a]		2.9		(90)		3.1	

OS, overall survival; PFS, progression-free survival; LRFS, local relapse-free survival; MMFS, multiple myeloma-free survival; S, surgery; RT, radiotherapy
[a] Median (year).
[b] 10-years MMFS rate (%).

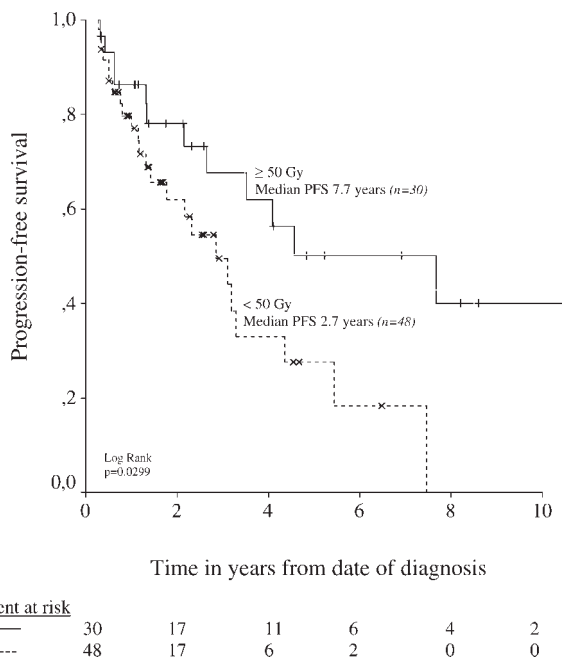

Figure 1. Kaplan-Meier plots on progression-free survival (PFS) time according to biologically equivalent dose at 2 Gy per fraction.

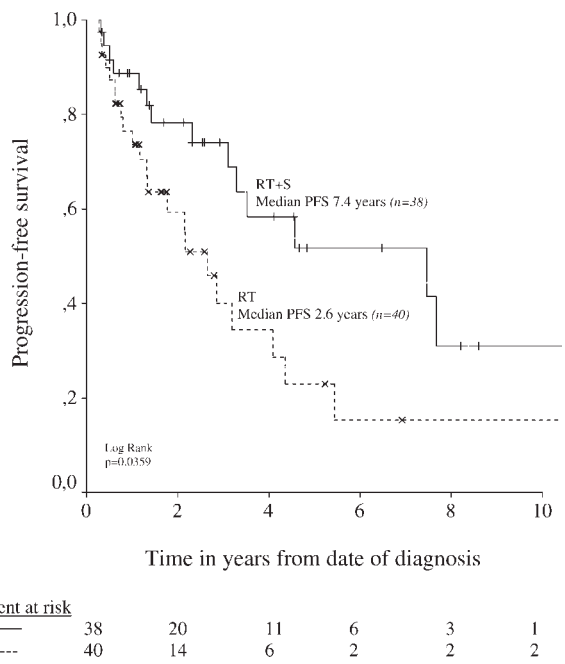

Figure 2. Kaplan-Meier plots on progression-free survival (PFS) time according to the type of treatment. S: surgery, RT: radiotherapy.

only the combination of surgery and radiation therapy and higher radiation doses were significantly associated with higher PFS. The hazard ratio was 0.197 (P = 0.035, 95% CI: 1.021–5.091) (Table IV). No differences were observed between SEP and SPB. There was no prognostic factor influencing MMFS in SEP subgroup.

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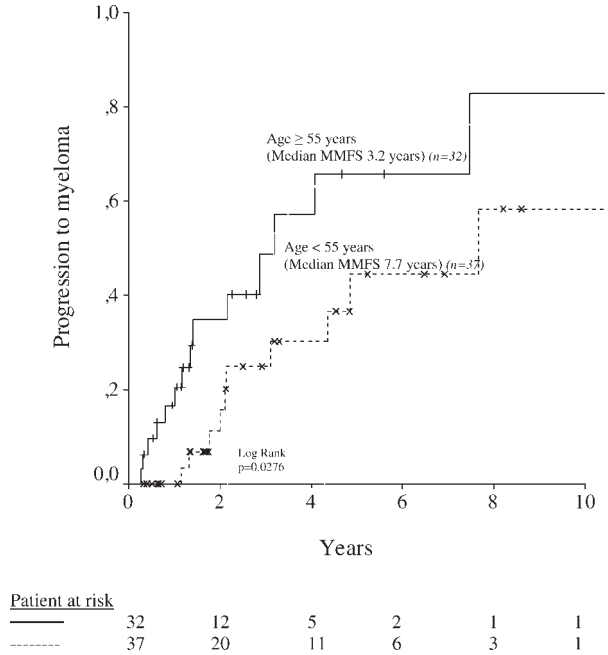

Figure 3. Kaplan-Meier plots on progression to myeloma according to age of the patients.

Local control

Local failure was observed in five patients with a mean time to local relapse of 1.5 years (range 0.28–12.03). Residual disease (on the soft tissue) did not disappear in one of these patients; increases were observed in the diameter and number of bone lesions in four of them. All of them received RT doses varying between 40 and 50 Gy. Two of them had lesions greater than 5 cm. In one of the five patients, the disease progressed to MM. Radiation doses of 40–50 Gy (not exceeding 50 Gy) in 20–25 fractions were delivered as 1.8–2 Gy per fraction. Four of them had macroscopic tumor before RT.

The 10-year local control (LC), probability was 94% in all patients, 94% in 57 patients with SPB, and 95% in 23 patients with SEP, respectively (Table III). On univariate analyses, there were no significant factors affecting LRFS in any of the patients or the subgroups with SPB or SEP (Tables III and IV).

Toxicity

No significant acute or late radiation toxicity was recorded. Three out of 59 recorded acute radiation toxicities according to the Common Toxicity Criteria version 2.0 were one grade 3 corneal toxicity and two grade 3 mucositis [34,35].

Discussion

In this study, we present a large series of patients with solitary plasmacytoma. With a median follow-up of 2.41 years, on multivariate analysis we found that none of the baseline factors we collected predicted for overall survival, that young age predicted for a better MMFS, and that both a higher dose of radiation and the combination of RT and surgery (rather than RT alone) predicted for better PFS. In terms of outcomes, the prognostic factors for the overall group and for the solitary plasmacytoma of bone group were similar with the exception of predictors for PFS. For this subset of patients with SBP, only treatment type affected outcomes whereas dose did not. Limitations of our study include the absence of complete baseline data including serum and urine monoclonal protein data, short follow-up, the retrospective nature of the study. No variable appeared to affect overall survival, but that finding may partially be due to the relatively short follow-up.

In this study, several differences were found between the SEP and SPB patients. The median ages were 47 and 54, respectively. The SEP patients were also more likely to be male, to have tumors located in the head and neck, to be operated on, to have smaller tumors before radiation, and to receive higher doses of radiation. There was a tendency in favor of SEP in terms of median PFS, although not significant. This could partially be because of limited sample size. In our study, most of the patient characteristics (median age, gender, site of tumor, the rate of SEP/SPB, etc.) are similar to the other plasmacytoma series in the literature [1,14,28,36].

Local control with RT is achieved in 80–100% of patients with plasmacytoma [28]. In our series, there was no significant difference between SEP and SPB in terms of local control. This could partially be because of limited sample size. The PFS probability for patients having head-neck lesion (most of which are known as SEP) was statistically significantly higher than the others without any difference in LC and this observation was supported in the literature [37]. Such a tendency, almost statistically significant, was also observed for MMFS in our study. This situation, although the prognostic value was not proved in multivariate analysis, seems to imply that the main problem in prognosis in especially medullary type plasmacytoma is that the disease is probably occult systemic [3,4,13,20].

The progression to MM has been reported to be more frequent in older patients, whose survival was also worse [3,17,26,37], but not reported by others [19,20,21,23]. In some series, no factors predictive of systemic recurrence could be identified [18,23,26,38]. We have verified in this study that old age is an independent prognostic factor for progression to MM ($P = 0.027$). This observation signals that instead of local treatment, some other factors like age may be more important in MM development. In this respect, the progress in prognostic factors that affect progression will contribute to determining patients, who need systemic treatment, and forming new treatment models [25].

Radiotherapy combined with surgery is an accepted treatment method depending on the resectability of the extramedullary lesion and may provide better results [11,12,15,16]. Adjuvant chemotherapy is debatable [28]. In a comprehensive review of more than 400 publications from 1905 to 1997, Alexiou et al. reported evidence that surgery alone gave the best results for SEP when negative surgical margins were obtained [10]. Our study shows that the combination of radiotherapy and surgery has a positive effect on PFS for overall group and SPB subgroup. The reason why the same effect could not be observed for SEP subgroup is probably the insufficient number of patients in the group or the need for a longer follow-up period.

In the study of Tsang et al., they indicated that patients with lesions <5 cm had a local control rate of 100% while patients with larger tumors had a rate of nearly 40% [17]. In some series, a lesion size of at least 4–5 cm was reported as the prognostic feature for conversion of SPB to multiple myeloma although this is controversial in the literature [3,17,20,27,37]. In our study, the statistically significant relation determined during on univariate analysis between "macroscopic" tumor existence prior to RT and both PFS and MMFS or the relation of the dimension of the tumor at diagnosis with prognosis could not be shown on multivariate analysis as an independent factor. It is similar for the analyses of SEP or SBP subgroup. This could partially be because of limited sample size. However, the observation

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that prior surgery treatment is an independent positive prognostic factor for PFS signals the importance of local tumor bulk for disease progression in patients receiving RT.

Strict RT dose guidelines are difficult to advice due to the limited number of patients and the absence of prospective randomized studies [28]. Some of the studies reported no-dose-response relationship in RT for plasmacytomas [3,20,36]; however, most of the authors suggested that a dose of 45–50 Gy is necessary for a high local control rate [9,16–19,26–28,39,40], mainly for soft tissue plasmacytomas [15]. Like our series, Frassica et al. showed no local failure for doses >50 Gy [26]. In our series, five local recurrences were observed, none of which received >50 Gy. Most of the patients received the accepted adequate dose for excellent local control of plasmacytoma [28,39,40]. Thus, it is expectable that dose differences in the present series did not affect LC significantly. Total RT dose showed a significant effect only on PFS, but not on LC and OS. This finding may partially be accounted for by the relatively short follow-up. Also, multivariate analyses revealed that radiation dose of >50 Gy was the independent factor predicting PFS, but not MMFS. The prognostic effect of higher RT dose could not be shown for SBP and SEP in the subgroup analyses.

However, the relationship between RT dose and PFS needs to be explained. This may be related, to some extent, to the nature of plasmacytoma, not to local relapse but systemic progression in prognosis of the disease, especially progression to MM, being the main problem. Moreover, MM development is likely to have relationship with factors like age rather than local treatment.

In conclusion, the diagnosis and staging of plasmacytoma using more specific histological, phenotypic, and radiographic criteria to exclude MM and other plasma cell neoplasm and conducting prospective studies with large series—especially evaluating SEP and SPB separately—will clarify the argument on prognostic factors and treatment of the disease.

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