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The predictive value of serum myeloma protein in solitary plasmacytoma

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Purpose: To identify the clinical usefulness of serum M protein and to establish a rationale for regular follow-up with serum protein electrophoresis in solitary plasmacytoma.

Materials and Methods: Sixty-nine patients with solitary plasmacytoma and solitary plasmacytoma with minimal marrow involvement according to the International Myeloma Working Group criteria were retrospectively reviewed.

Results: At a median follow-up of 6.2 years, 5-year local control (LC), 5-year multiple myeloma-free survival (MMFS), 5-year failure-free survival (FFS), and 5-year overall survival (OS) were 82.6%, 44.1%, 41.8%, and 85.1%, respectively. Among the patients whose initial serum M protein was present or not evaluated, 37.3% of patients showed disappearance of serum M protein after various treatment. MMFS of these patients were comparable to non-secretory plasmacytoma with undetectable levels of M protein, and significantly better than patients with persistent M protein. Increase of serum M protein ≥0.1 g/dL was most predictive of treatment failure with area under the curve of 0.731.

Conclusion: Patients who eventually showed persistence of serum M protein after treatment showed worse MMFS and FFS compared to those whose serum M protein disappeared or who had initially non-secretory disease. The increase of serum M protein level ≥0.1 g/dL from current nadir was predictive of treatment failure. Therefore, regular follow-up with serum M protein is highly recommended especially unless the patient had initially non-secretory disease.

Keywords: Plasmacytoma, Myeloma protein, Risk factor, Radiotherapy

Introduction

Solitary plasmacytoma is a rare disease which accounts for less than 10% of plasma cell neoplasm [1]. It is diagnosed at a median age of 60 and is a male-dominant disease with a male to female ratio of approximately 2:1 [2,3]. Solitary plasmacytoma is subdivided into two disease entities. Solitary plasmacytoma originating from bones are classified as solitary plasmacytoma of the bone (SPB), whereas soft tissue origin plasmacytoma is classified as solitary extramedullary plasmacytoma (SEP). While SPB is most frequently observed in the axial skeleton, such as vertebra, SEP is commonly found in the head and neck, especially in the upper aerodigestive tract [2,3].

Owing to its rarity, there were no randomized trials to identify the standard treatment for solitary plasmacytoma. Although multiple myeloma (MM) is generally treated with chemotherapy and is thought to be incurable, solitary plasmacytoma is treated well with excellent 5-year local control (LC) rate ranging from 81 to 95% af-

ter local radiation therapy (RT) [4–6]. Although there is no consensus regarding the optimal dose of RT, but RT dose ≥40 Gy was reported to improve LC [4,7]. Nevertheless, more than half of the patients after local or systemic treatment eventually progress to MM with long-term follow-up [3,4,8,9].

Although there is a consensus criteria for treatment response assessment for multiple myeloma [10], there is no widely used criteria for solitary plasmacytoma. Also, the prediction of treatment failure in solitary plasmacytoma patients is not available although early predictions of treatment failure is important considering the high rates of progressions to MM in order to make early salvage treatment possible.

Myeloma protein, which is also called M protein, is an abnormal protein produced in excess by an abnormal monoclonal proliferation of plasma cells and is typically detected in serum or urine of patients with MM or plasma cell tumors. Although only 3% of MM patients are non-secretory [11], i.e., no detectable serum and urine M protein at diagnosis, M protein is present in only 33% to 64% of solitary plasmacytoma patients at diagnosis [4,5,12,13]. Also in patients with M protein, the median level of serum M protein at diagnosis of solitary plasmacytoma patients is less than 1 g/dL [5,13], which is lower than that of MM (>3 g/dL) [11]. Nevertheless, the measurements of serum M protein level for solitary plasmacytoma is important in that the persistence of serum M protein after treatment was associated with poor prognosis [12–14] and therefore, the European Expert Panel recommended serum and urine electrophoresis and immunofixation to be performed during follow-up [15].

However, the usefulness of serum M protein as a biomarker to assess treatment response and to predict treatment failures in solitary plasmacytoma is yet to be studied. In MM, randomized trials implemented the increase in serum M protein more than 0.5 g/dL from nadir to define disease progression [16,17]. Considering the high incidence of non-secretory plasmacytoma and low level of serum M protein level at diagnosis, this criterion seems not to be appropriate for solitary plasmacytoma. Therefore, we tried to identify the clinical usefulness of serum M protein for predicting treatment failures and to establish a rationale for regular follow-up with serum protein electrophoresis to evaluate serum M protein level.

Materials and Methods

1. Patients and diagnostic work-up

Medical records of patients with solitary plasmacytoma and solitary plasmacytoma with minimal marrow involvement according to the International Myeloma Working Group (IMWG) criteria [18] were retrospectively reviewed. A total of 69 solitary plasmacytoma patients who were taken care of between 1986 and 2019 at Seoul National University Hospital and Seoul National University Bundang Hospital were identified. At initial diagnostic work-up, all patients were evaluated with at least one radiological imaging work-ups (100.0%) including simple X-ray, CT, MRI, bone scan, or FDG-PET scan and laboratory work-ups including serum protein electrophoresis (62.3%), urine protein electrophoresis (55.1%), and serum free light chain ratio (31.9%).

The characteristics of all patients are shown in Table 1. The median age at the diagnosis of solitary plasmacytoma was 60.5 years (range, 29.7 to 79.8 years) and male was predominant (59.4%). The most common initial presenting symptom was pain at the involved site (59.4%). Vertebra was the most common primary site of the 51 SPB patients. Head and neck was the most common primary site of the 18 SEP patients. At initial diagnostic work-up, serum M protein, Bence Jones proteinuria, and abnormal free light chain ratio was present in 58.1%, 15.8%, and 50.0% of patients whose pre-treatment data was available, respectively. Patients treated with surgery alone or surgery plus adjuvant RT included more patients with insufficient initial work-up studies including serum and urine protein electrophoresis ($p < 0.05$) (Supplementary Table S1).

2. Treatment and follow-up

All patients received a curative treatment; definitive RT alone (46.4%), surgical resection (24.6%), and surgical resection plus adjuvant RT (17.4%). The median total radiation dose was 45.0 Gy (range, 23.4 to 70.0 Gy). Curative surgical resection was performed in 33 patients (47.8%) and 90.9% of them underwent complete resection. Chemotherapy was administered to 8 patients (11.6%). After the completion of treatment, patients were followed up with work-ups including radiological imaging studies, serum protein electrophoresis, and serum free light chain ratio. The median time from the initial serum protein electrophoresis at the time of diagnosis to first post-treatment serum protein electrophoresis was 3.5 months (range, 1.3 to 36.5 months). In this study, we defined the "disappearance of serum M protein" in order to assess treatment response. When post-treatment serum M protein of a patient whose initial serum M protein was present or not evaluated was measured and showed no detectable serum M protein during follow-up, it was regarded as disappearance of serum M protein.

Patients were defined as progression to MM, whenever meeting the criteria of IMWG for the diagnosis of MM during follow-up [18]. The diagnosis of MM requires clonal bone marrow plasma cells ≥10% or a biopsy-proven plasmacytoma plus the presence of one or more myeloma-defining events. Myeloma defining events include the presence of hypercalcemia, renal insufficiency, anemia, and bone lesion. Also, clonal bone marrow plasma cells ≥60%, se-

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Table 1. Patient characteristics of solitary plasmacytoma

Characteristic	Number of patients (%)
Age (yr)	
< 60	32 (46.4)
≥ 60	37 (53.6)
Sex	
Male	41 (59.4)
Female	28 (40.6)
Site of lesion	
SPB	51 (73.9)
Craniofacial bone	11 (15.9)
Vertebra	21 (30.4)
Pelvic bone	9 (23.1)
Extremity	4 (5.8)
Others	6 (8.7)
SEP	18 (26.1)
Head and neck	14 (20.3)
Others	4 (5.8)
Anaplastic histology	
No	67 (97.1)
Yes	2 (2.9)
Serum M protein at diagnosis (g/dL)	
0	18 (26.1)
0.1–1.0	11 (15.9)
≥ 1.1	14 (20.3)
Unknown	26 (37.7)
Type of M protein	
IgG	18 (72.0)
Light chain only	2 (8.0)
Unknown	5 (20.0)
Bence Jones proteinuria	
Absent	32 (46.4)
Present	6 (8.7)
Unknown	31 (44.9)
Serum free light chain ratio	
Normal	11 (15.9)
Abnormal	11 (15.9)
Unknown	47 (68.1)
Treatment	
RT only	32 (46.4)
Surgery only	17 (24.6)
Surgery + RT	12 (17.4)
Chemotherapy alone	3 (4.3)
RT + chemotherapy	2 (2.9)
Surgery + chemotherapy	1 (1.4)
Surgery + RT + chemotherapy[a]	2 (2.9)
Radiation therapy[b]	
No radiation therapy	22 (31.9)
< 45 GyEQD2	31 (44.9)
≥ 45 GyEQD2	15 (21.7)
Surgical resection	
No surgical resection	36 (52.2)
Partial resection	3 (7.7)
Complete resection	30 (43.5)

SPB, solitary plasmacytoma of bone; SEP, solitary extramedullary plasmacytoma; RT, radiation therapy; EQD2, equivalent dose in 2-Gy fractions at α/β of 10.
[a]One patient received additional radiosurgery.
[b]One patient with unknown dose excluded.

rum free light chain ratio ≥ 100, or more than one focal lesion on MRI are diagnosed as MM regardless of the presence of myeloma defining event.

3. Statistical analysis

The characteristics according to various treatments were compared using Fisher's exact test. The actuarial LC, multiple myeloma-free survival (MMFS), failure-free survival (FFS), and overall survival (OS) were calculated with Kaplan-Meier analysis. All survivals were calculated from the first day of initial treatment. The events were local failure before progression to MM for LC, progression to MM or death from any cause for MMFS, any failure or death from any cause for FFS, and death from any cause for OS. Log-rank test was used for univariate analysis of the prognostic factors. Based on prognostic factors with $p < 0.05$, multivariate analysis was conducted. To identify a set of independent predictive factors a multivariate analysis with Cox proportional hazards model or Cox regression with Firth's penalized likelihood was performed as appropriate. In all analyses $p < 0.05$ was considered statistically significant. All statistical analyses were conducted in R version 3.5.0.

Results

1. Survival outcome and cause of death

At a median follow-up of 6.8 years (range, 0.1 to 29.3 years), 9 patients (13.0%) experienced a local failure; 8 within 3 years and one at 9 years after treatment (Fig. 1A). The 5- and 10-year LC rate were 82.6% and 68.9%. The LC rates did not differ significantly across treatment modalities. Anaplastic plasmacytoma was the only prognostic factor for LC (Table 2, 3). In the meanwhile, RT improved LC for extramedullary lesions (100.0% vs. 53.6%; $p = 0.028$).

Overall, 32 patients (46.8%) progressed to MM. Most of the progressions to MM (96.9%) occurred within the first 5 years after treatment. The 5- and 10-year MMFS were 44.1% and 36.7%. In univariate analysis and multivariate analysis, SPB (hazard ratio [HR] = 8.63, $p = 0.036$), tumor size ≥ 5 cm (HR = 2.84, $p = 0.012$), and anaplastic histology (HR = 50.9, $p = 0.002$) were adverse prognostic factors for MMFS (Tables 2, 3). The 5- and 10-year FFS were 41.8% and 34.9%. As they were for MMFS, SPB (HR = 10.3, $p = 0.023$), tumor size ≥ 5 cm (HR = 2.18, $p = 0.043$), and anaplastic histology (HR = 66.6, $p = 0.001$) were significant adverse prognostic factors for FFS in the univariate and multivariate analysis (Tables 2, 3). The median OS was 14.0 years (95% confidence interval [CI], 11.8 years to upper limit not reached). The 5- and 10-year OS were 85.1% and 70.6%. There was no significant prognostic factor for OS (Table 4).

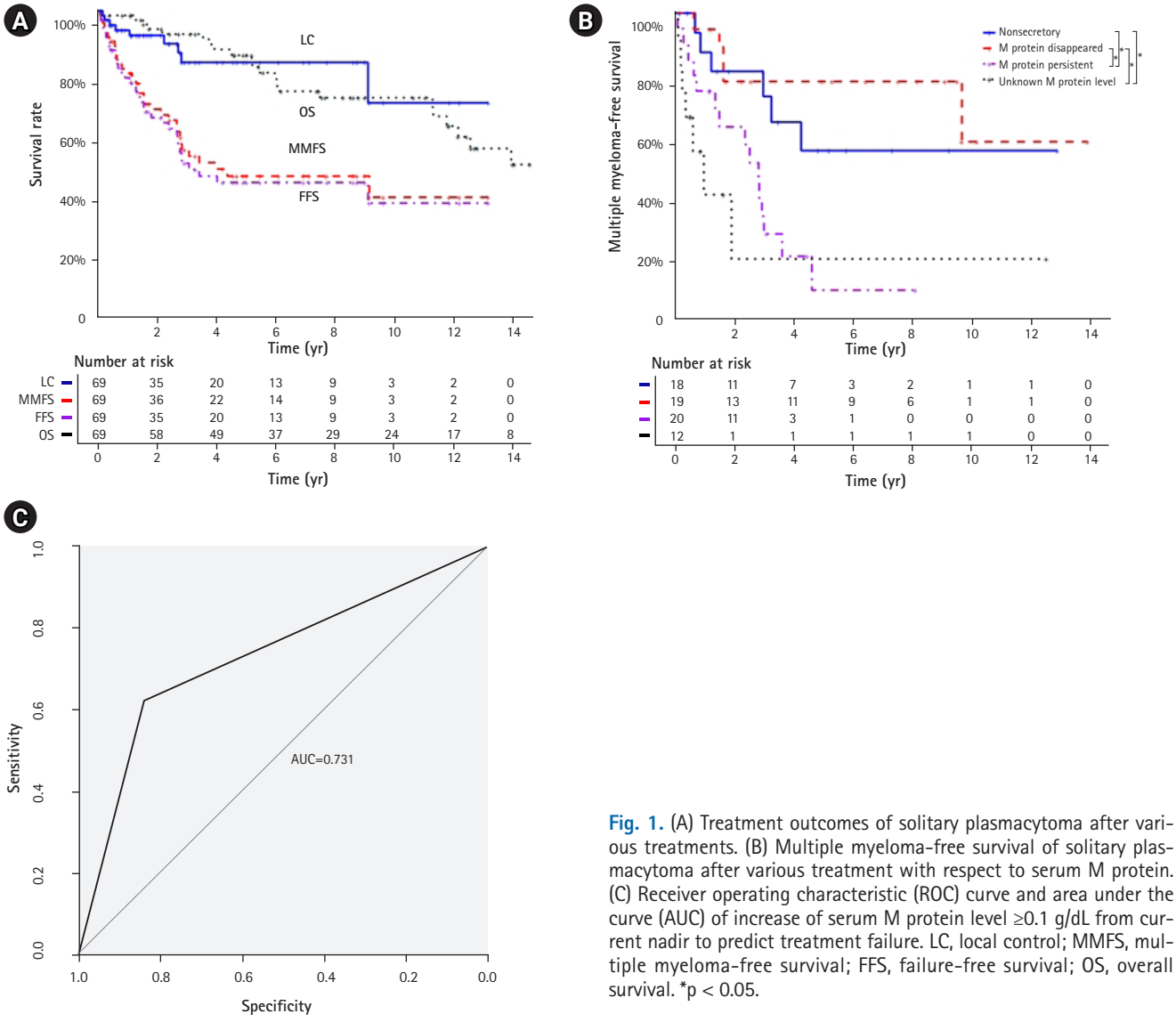

Fig. 1. (A) Treatment outcomes of solitary plasmacytoma after various treatments. (B) Multiple myeloma-free survival of solitary plasmacytoma after various treatment with respect to serum M protein. (C) Receiver operating characteristic (ROC) curve and area under the curve (AUC) of increase of serum M protein level ≥0.1 g/dL from current nadir to predict treatment failure. LC, local control; MMFS, multiple myeloma-free survival; FFS, failure-free survival; OS, overall survival. *p < 0.05.

At the time of the analysis, 22 deaths (31.9%) were reported, and 6 patients died from the progression of MM. There were two deaths related to treatments; one from complications after surgical resection and another from side effects of salvage chemotherapy. Five deaths were unrelated to plasmacytoma or treatment and the cause of death of remaining 9 patients was unknown.

2. Prognostic factors in patients treated with RT

In the subgroup of patients treated with any treatment that includes RT, tumor location, tumor size, and serum free light chain ratio were significant prognostic factors for MMFS and FFS in the univariate analysis. In the multivariate analysis, SPB (HR = 22.1, p < 0.001), tumor size ≥5 cm (HR = 2.64, p = 0.045), and abnormal serum free light chain ratio (HR = 6.29, p = 0.008) were associated with poor MMFS. For FFS, SPB (HR = 22.7, p < 0.001) and abnormal serum free light chain ratio (HR = 7.38, p = 0.003) were statistically significant adverse prognostic factors. However, there were no significant prognostic factors identified for LC and OS for patients treated with RT. The addition of surgical resection, chemotherapy, or RT dose ≥45 GyEQD2 did not result in significantly improved prognosis.

3. Disappearance of serum M protein after treatment as a prognostic factor

At the time of diagnosis, 18 patients were non-secretory. Among the remaining 51 patients who had serum M protein or whose pre-treatment serum M protein level was not evaluated, serum M protein disappeared in 19 patients after a median period of 2.4 months (range, 0.0 to 51.1 months) following treatment. The 5-year MMFS of patients with non-secretory plasmacytoma, disap-

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Table 2. Risk factors associated with treatment outcome of solitary plasmacytoma (univariate analysis)

	Number of patients	5-yr LC (%)	p-value	5-yr MMFS (%)	p-value	5-yr FFS (%)	p-value	5-yr OS (%)	p-value
Age (yr)									
< 60	32	68.7	0.150	40.8	0.680	37.3	0.550	89.5	0.320
≥ 60	37	94.3		47.4		45.9		81.5	
Sex									
Male	41	72.5	0.130	37.4	0.220	34.0	0.098	85.8	0.190
Female	28	94.4		53.4		53.4		84.2	
Tumor location									
Extramedullary	18	80.2	0.820	80.2	0.007	80.2	0.004	94.4	0.120
Bone	51	82.9		32.1		29.4		81.2	
Tumor size (cm)									
< 5	33	83.8	0.710	70.2	< 0.001	63.7	0.001	93.2	0.076
≥ 5	30	87.1		22.6		22.8		74.9	
Anaplastic histology									
No	67	85.4	< 0.001	45.5	0.001	43.1	< 0.001	84.6	0.260
Yes	2	0.0		0.0		0.0		100.0	
Serum M protein present									
No	18	90	0.470	55.7	0.220	55.7	0.130	87.1	0.650
Yes	25	85.2		27.3		29.2		79.8	
Unknown	26	77.0		47.8		43.1		88.1	
Bence Jones proteinuria									
Absent	32	88.0	0.160	37.9	0.820	39.2	0.790	85.2	0.890
Present	6	100.0		50.0		50.0		100.0	
Unknown	31	74.1		49.1		43.2		82.9	
Serum free light chain ratio									
Normal	11	100.0	0.320	67.5	0.046	67.5	0.019	90	0.910
Abnormal	11	78.8		21.8		18.2		75.0	
Unknown	47	79.6		45.2		43.0		86.3	
Treatment									
RT alone	32	79.8	0.340	31.3	0.560	31.4	0.530	83.6	0.260
Surgery alone	17	72.9		55.8		49.0		94.1	
Surgery + RT	12	100		50.9		50.9		75.0	

LC, local control; MMFS, multiple myeloma-free survival; FFS, failure-free survival; OS, overall survival; RT, radiation therapy.

Table 3. Risk factors associated with treatment outcome of solitary plasmacytoma (multivariate analysis)

	LC		MMFS		FFS	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Tumor location						
Extramedullary	-		Ref.	0.036	Ref.	0.023
Bone	-		8.63 (1.15–64.9)		10.28 (1.37–76.9)	
Size of lesion (cm)						
< 5	-		Ref.	0.012	Ref.	0.043
≥ 5	-		2.84 (1.26–6.42)		2.18 (1.03–4.65)	
Anaplastic histology						
No	Ref.	< 0.001	Ref.	0.002	Ref.	0.001
Yes	50.6 (7.01–366)		50.9 (4.14–626)		66.6 (5.39–822)	

LC, local control; MMFS, multiple myeloma-free survival; FFS, failure-free survival; HR, hazard ratio; CI, confidence interval.

pearance of serum M protein, persistence of serum M protein, and unknown post-treatment serum M protein level were 55.7%, 78.0%, 10.8%, and 20.8%, respectively (Fig. 1B). The MMFS of non-secretory plasmacytoma patients and patients whose serum M protein disappeared were comparable ($p > 0.05$). Both groups of patients showed significantly superior 5-year MMFS compared to patients who showed persistence of serum M protein and patients whose serum M protein level was not evaluated during follow-up ($p < 0.05$).

4. Correlation of disappearance of serum M protein and RT

Among patients who initially had serum M protein, the post-treatment serum M protein level was available from 20 patients. Two patients who did not receive RT showed persistence of serum M protein after treatment, whereas disappearance of serum M protein was observed in 7 patients (38.9%) after RT (Table 3). The rates of disappearance of serum M protein were 25.0% and 66.7% with RT dose < 45 GyEQD2 and ≥ 45 GyEQD2, respectively.

5. The increase of serum M protein level as a predictive marker for treatment failure

Next, we tried to predict treatment failures with the level change of serum M protein. Overall, 40 patients were followed up with at least two serum protein electrophoresis tests during follow-up before any treatment failure, defined as local failure and progression to MM. The median value of post-treatment nadir value of serum M protein was 0.0 g/dL (range, 0.0 to 3.2 g/dL). During follow-up, 17 patients experienced an increase of serum M protein level at least once before clinically detected treatment failure. The median of maximum increase of serum M protein from nadir was 0.7 (range, 0.02 to 2.1 g/dL).

Considering the high incidence of non-secretory M protein and low level of serum M protein in solitary plasmacytoma at diagnosis, we evaluated the increase of serum M protein level ≥ 0.1 g/dL from current nadir instead of 0.5 g/dL, which is implemented in MM, to predict treatment failure. The area under the curve (AUC) of the prediction model with this criterion was 0.731 (Table 5, Fig. 1C). Specificity and sensitivity of this model were 84.2% and 61.9%, respectively. The median time to treatment failure from the day serum M protein level increased 0.1 g/dL or more from current nadir was 16.9 months (95% CI, 6.9 months to upper limit not reached).

In addition, three other criteria were evaluated, which are two increases of serum M protein level, two consecutive increases of serum M protein level, and increase of serum M protein above double the value of nadir. The AUC of the prediction models with these criteria were 0.690, 0.662, and 0.614, respectively (Table 5). As the increase of serum M protein level ≥ 0.1 g/dL from current nadir showed highest AUC amongst the four criteria compared, we adopted this criterion to predict treatment failure.

Table 4. Correlation of disappearance of serum M protein and radiation therapy

RT dose[a]	Number of patients	Serum M protein	
		Disappearance (%)	Persistence (%)
No RT	2	0 (0.0)	2 (100.0)
< 45 GyEQD2	12	3 (25.0)	9 (75.0)
≥ 45 GyEQD2	6	4 (66.7)	2 (33.3)

RT, radiation therapy; EQD2, equivalent dose in 2-Gy fractions at α/β of 10.
[a]One patient with unknown dose excluded.

Discussion and Conclusion

In this study, we evaluated the prognostic value of serum M protein level at diagnosis and its level change or conversion during follow-up to assess treatment response and predict treatment failures of solitary plasmacytoma.

Prognostic factors with contradictory prognostic values for solitary plasmacytoma were demonstrated in previous studies due to different treatment profiles and small number of patients included in each study. Although local control was excellent in this study and was also consistent with that of previous studies, progression to MM remained to be the main obstacle for failure-free survival as observed in Fig. 1A. In this study, SPB and tumor size ≥ 5 cm were associated with poor MMFS and FFS, which is consistent with the results of previous studies [3,5,8,9,19,20]. Older age [3,5,19–21], the abnormal post-treatment free light chain ratio [12], the pres-

Table 5. Correlation of various increases of serum M proteins with treatment failure

	Number of patients (%)	Sensitivity (%)	Specificity (%)	AUC	Median time to treatment failure (mo)
Increase ≥ 0.1 g/dL from current nadir	16 (40.0)	61.9	84.2	0.731	16.9
Two increases	13 (37.1)	55.6	82.4	0.690	20.8
Two consecutive increases	12 (34.3)	50.0	82.4	0.662	17.4
Increase double above nadir	9 (22.5)	33.3	89.5	0.614	4.0

AUC, area under the curve.

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ence of serum M protein at diagnosis [5] and after treatment [12] were also suggested to be associated with poor prognosis. Warsame et al. [22] reported clonal plasma cells in BM, presence of urine Bence Jones protein, and higher RT dose as adverse prognostic factors for progression-free survival.

In addition to SPB and tumor size ≥5 cm, anaplastic plasmacytoma was associated with poor LC, MMFS, and FFS. Anaplastic plasmacytoma is an extremely rare type of plasmacytoma which can develop in patients with immunosuppression and combined Epstein-Barr virus infection [23]. However, because of its rarity the clinical course of anaplastic plasmacytoma is unknown. In this study, two patients of anaplastic plasmacytoma were included and they showed rapid local failure and progression to MM. However, both patients survived more than 10 years. It seems that anaplastic plasmacytoma shows rapid progression but does not result in poor overall survival, but the clinical course of anaplastic plasmacytoma needs to be investigated with larger number of patients.

In this study, patients with non-secretory plasmacytoma and patients whose serum M protein disappeared after treatment showed superior MMFS compared to patients who had persistent serum M protein after treatment. However, the prognostic value of serum M protein level at diagnosis is controversial. Non-secretory plasmacytoma showed better MMFS in the study by Reed et al. [5], whereas the opposite result showing that non-secretory plasmacytoma is associated with worse MMFS and cause-specific survival was also reported [13,14]. In contrast, the persistence of M protein after treatment is uniformly reported to be associated with poor MMFS [12–14], which was also observed in this current study. Moreover, we showed the usefulness of the increase of serum M protein level ≥0.1 g/dL from current nadir for predicting treatment failures. Therefore, it would be reasonable to follow-up patients, who initially had serum M protein or whose pre-treatment serum M protein level was not evaluated, with a regular serum protein electrophoresis test along with radiologic examinations until the serum M protein disappears. In addition, even if patients had non-secretory disease or their serum M protein disappeared, a regular follow-up with serum protein electrophoresis would be needed in order to make earlier detection and salvage treatment possible.

Immunofixation and free light chain ratio are another tests to evaluate serum M protein. It has been reported that 9.7% of normal serum protein electrophoresis showed positive immunofixation result [24] and therefore, immunofixation could be a good complementary test when combined with serum protein electrophoresis during follow-up. Abnormal serum free light chain ratio was a significant prognostic factor in patients who were treated with RT in our study and in a previous study [12]. Considering this, serum free light chain ratio could be another potential predictive biomarker to be investigated and utilized.

RT has been known as the treatment of choice for solitary plasmacytoma [15,25,26] with evidences from retrospective studies showing improved LC [3], disease-free survival [3], and OS [2] with RT. Regarding the dose of RT, higher doses were recommended for SEP [27] and larger tumors [19], although no definite dose-response relationship for RT >30 Gy was observed in another study [3]. In this study, we also could not find a definite dose-response relationship. However, RT ≥45 GyEQD2 seemed to increase the rates of disappearance of serum M protein, which can be interpreted as good treatment response, although the number of patients were insufficient to show definite relationship.

In this study, since solitary plasmacytoma without evidence of MM is very rare in nature, we could find only a small number of patients. Patients who were incidentally diagnosed as solitary plasmacytoma after surgical resection lacked the pre-treatment work-up for solitary plasmacytoma as shown in Supplementary Table S2. Therefore, our definition of disappearance of serum M protein included patients whose initial serum M protein level was not evaluated when predicting the prognosis with respect to serum M protein level. However, considering that it is often the case that solitary plasmacytoma is incidentally diagnosed after surgery, as it was in this study, it would be still meaningful to include patients whose initial serum M protein was not evaluated and predict their prognosis. Also, the data of proportion of clonal plasma cells in the bone marrow was not available in 46.4% of the patients and therefore, we could not show any prognostic difference between solitary plasmacytoma and solitary plasmacytoma with minimal marrow involvement according to the IMWG criteria. However, with long-term follow-up data, we could derive a meaningful conclusion regarding the clinical value of serum M protein level, although further studies with larger number of patients are needed for validation.

In conclusion, we found that patients who eventually showed persistent serum M protein after treatment had worse prognosis compared to those whose serum M protein disappeared or initially had non-secretory disease. Also, the increase of serum M protein level ≥0.1 g/dL from current nadir was predictive of treatment failure. Therefore, we recommend a regular follow-up with serum protein electrophoresis after the treatment of solitary plasmacytoma to assess treatment response and predict treatment failure. Also, closer follow-up with serum protein electrophoresis is needed for patients who initially had serum M protein or whose serum M protein level was not evaluated.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Supplementary Materials

Supplementary materials can be found via https://doi.org/10.3857/roj.2019.00570

Table S1. Risk factors associated with treatment outcome of solitary plasmacytoma treated with RT (univariate analysis)

Table S2. Characteristic of the patients according to their treatments

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