wjpmr, 2021,7(6), 70-75

SJIF Impact Factor: 5.922

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Research Article

ISSN 2455-3301

WJPMR

SOLITARY BONE PLASMACYTOMA: EXPERIENCE OF THE NATIONAL INSTITUTE OF ONCOLOGY IN RABAT

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Article Received on 06/04/2021 **Article Revised on 27/04/2021** **Article Accepted on 17/05/2021**

ABSTRACT

We reported 10 years of experience from our institution, which included 19 patients followed for solitary bone plasmacytoma treated by radiotherapy alone or in addition to surgery. This retrospective study aimed to assess the therapeutic results of these tumors in terms of local control and overall survival and to assess their diagnostic, therapeutic, and evolutionary aspects. All patients received radiation therapy. This irradiation was exclusive in 100% of cases or adjuvant to laminectomy in 57.9%. The mean dose of radiotherapy was 44.02Gy ± 5.35 and this was delivered by a three-dimensional conformational radiotherapy-type technique in 19 patients. After a median follow-up of 4.5 years (2-13.5), local control, defined by radiological stability, was obtained in the 19 patients, 3 patients presented with a multifocality. The 31-month progression-free survival rate was 70.8% and the 82-month overall survival rate was 60.6%. Radiotherapy is the standard treatment for solitary bone plasmacytoma. It ensures local control in 90% of cases. The prognosis is affected by the progression to multiple myeloma, which justifies careful monitoring after treatment and suggests reflection on the exact place of chemotherapy. **Résumé:** Nous avons rapporté 10 ans d'expérience de notre institution ayant inclus 19 patients suivis pour un plasmocytome solitaire osseux traités par radiothérapie seule ou associée en complément à la chirurgie. Le but de cette étude rétrospective était d'évaluer les résultats thérapeutiques de ces tumeurs en termes de control local et de survie globale et d'évaluer ses aspects diagnostics, thérapeutiques et évolutifs. Tous les patients ont reçu une radiothérapie. Cette irradiation a été exclusive dans 100% des cas ou adjuvante à une laminectomie dans 57,9%. La dose moyenne de la radiothérapie était de 44,02Gy ± 5,35 et celle-ci a été délivrée par une technique de type de radiothérapie conformationelle tridimensionnelle chez 19 patients. Apres un suivi médian de 4,5ans (2-13,5), le contrôle local, défini par une stabilité radiologique, a été obtenu chez les 19 patients, 3 patients ont présentés une multifocalité. Le taux de survie sans progression à 31 mois était de 70,8% et le taux de survie globale à 82 mois était de 60,6%. La radiothérapie constitue le traitement de référence du plasmocytome osseux solitaire. Elle permet d'assurer le contrôle local dans 90 % des cas. Le pronostic est affecté par l'évolution vers le myélome multiple, ce qui justifie une surveillance rigoureuse après traitement et suggère une réflexion sur la place exacte de la chimiothérapie.

INTRODUCTION

Solitary plasmacytoma is defined as an isolated plasma cell proliferation derived from a single clone of more or less differentiated B lymphocytes. It is a rare entity that presents in relation to the localization of two clinical forms: solitary bone or intramedullary plasmacytoma (as a single bone lesion) and solitary extramedullary plasmacytoma (localized in soft tissue). Solitary bone plasmacytoma is the most frequent and its evolution to multiple myeloma, described in the literature in 55% of cases, still calls into question its nosological authenticity. The standard treatment is external radiotherapy, sometimes combined with surgery.

MATERIALS AND METHODS

This is a retrospective descriptive study of 19 patients followed in the radiotherapy department of the National Institute of Oncology of Rabat for a solitary bone plasmacytoma between January 2010 and December 2017.

The data were extracted from the medical records of patients whose numbers were indexed from the Excel database of the register of the epidemiology unit of the Institute.

All patients with the following criteria were included in this study.

• a biopsy of the positive bone lesion allowing the diagnosis of a plasma cell tumor
• a radiological and/or metabolic assessment to confirm the uniqueness of the bone lesion
• a medullary plasmacytosis of less than 10%.

The initial workup included a blood count, electrophoresis and immunoelectrophoresis of serum proteins, phosphocalcic workup, testing for Bence Jones proteinuria, and a medullogram.

Patients who did not have all of these criteria necessary for a definite diagnosis were excluded.

Target volumes: Anatomo-clinical target volume was the macroscopic tumor volume with one or two vertebrae on either side in the event of spinal involvement and a margin of 1 cm to 3 cm around the other locations. The predicted target volume was the anatomo-clinical target volume plus 0.5 to 1 cm.

The follow-up was biological (blood count, immunoelectrophoresis of proteins, sedimentation rate) and radiological.
We used for data entry and statistical analysis, the statistical software for the social sciences (SPSS) version 13.0.

Local control and survival rates were estimated using the Kaplan-Meier method and the comparison of curves in univariate or multivariate analysis was performed by the log-rank test and by the proportional hazards regression model by Cox. The significance level was 5%.

RESULTS

The mean age of our patients was 56.84 ± 13.11.

Of the 19 patients, 11 were men and 8 were women.
The median time to diagnosis was 9 months (range: 3 - 14 months)
The telltale symptoms were pain (100%) followed by spinal cord compression (57.89%).
The spine was the most frequent lesion site (13 cases) followed by the sacrum (3 cases), rib (1 case), iliac bone (1 case), tibia (1 case).
8 patients had a monoclonal peak on protein electrophoresis.
All patients received associated external radiotherapy associated with surgery (laminectomy) in 11 cases (57.9%).
The mean dose was 44.02 Gy ± 5.35 and this was delivered by a three-dimensional conformal radiotherapy type technique.
Patient and tumor characteristics are shown in Table 1.
Local control, defined by radiological stability, was observed in 19 patients.
Multifocality, defined by the appearance of one or more lesions without bone marrow plasmacytosis. It was observed in 3 patients in our study with a mean delay of 48.66 months.
Myeloma transformation was retained if, in addition to other bone lesions, the sternal puncture or bone marrow biopsy showed plasmacytosis of more than 10%. In our sample, 5 patients had progressed to multiple myeloma.
The 31-month progression-free survival rate was 70.8% and the 82-month overall survival rate was 60.6% (Figures 1 and 2)
In multivariate statistical analysis, no factor was significantly correlated with progression-free survival (PFS) or overall survival (OS). (Table 2).

Tables and Figures

Table 1: Descriptive characteristics of our studied series.

Characteristics (N = 19)	**Values**
Age (years) *	56,84 ± 13,11
Sex **	
Man	11 (57,9)
Women	8 (42,1)
Bence Jones protein expression **	
Positive	5 (26,3)
Negative	14 (73,7)
Anatomical location of the plasmacytoma **	
Spine	13 (68,42)
Coast	1 (5,26)
Iliac bone	1 (5,26)
Sacrum	3 (15,8)
Tibia	1 (5,26)
Time to diagnosis &	9 [3 - 14]
Treatment **	
Surgery	11 (57,9)
Radiotherapy	19 (100)
Dose *	44,02 ± 5,35

* expressed as mean and standard deviation

** expressed in number and percentage
& expressed as median – quartiles

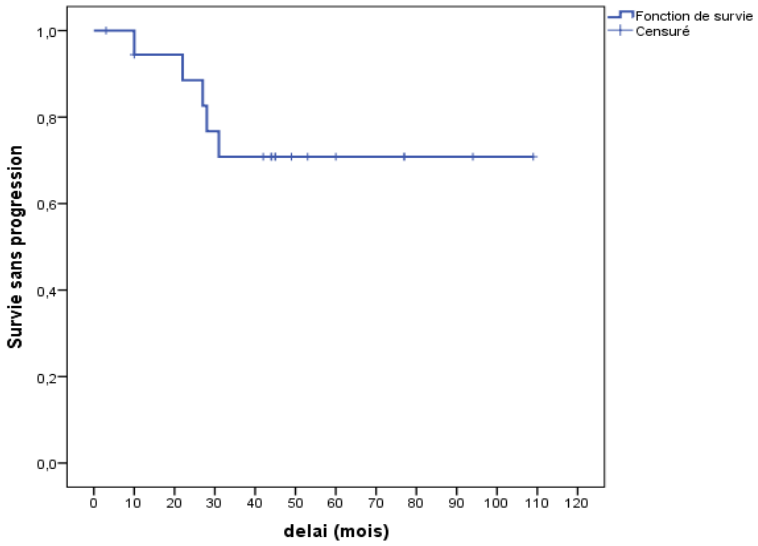

Figure 1: Kaplan-Meier estimates of the progression-free survival curve of solitary bone plasmacytomas treated with radiotherapy.

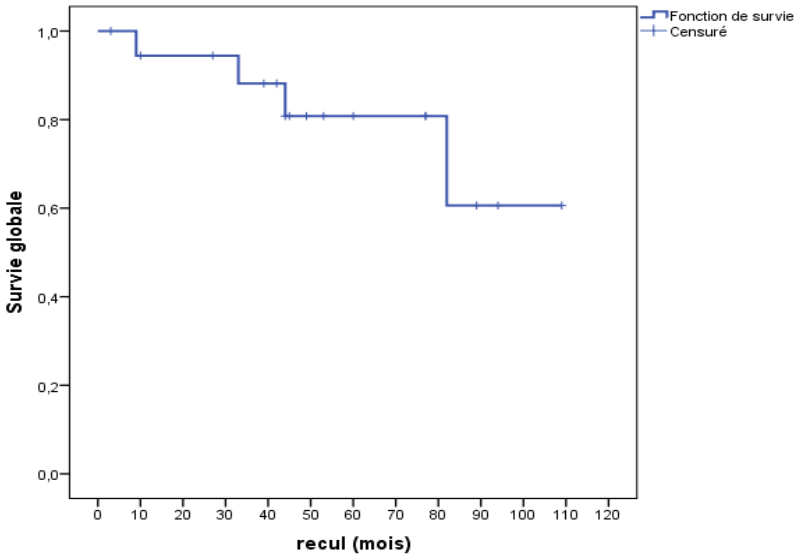

Figure 2: Kaplan-Meier estimates of the overall survival of solitary bone plasmacytomas treated with radiotherapy.

Table 2: Multivariate analysis of factors that may influence progression-free survival and Overall Survival.

Variables in the equation

	p	HR	95,0% IC pour Exp(B)	
			Inférieure	Supérieure
AGEq	,517	,520	,072	3,750
PIC	,391	2,927	,252	34,047
locatQ	,929			
locatQ(1)	,702	,638	,064	6,355
locatQ(2)	,986	,000	,000	.

DISCUSSION

Solitary plasmacytoma is a rare tumor, accounting for less than 5% of plasma cell neoplasms.[1, 2] It is defined by the existence of a localized infiltrate of malignant plasma cells; without systemic proliferative plasma cell involvement.[3] There are two clinical forms of solitary plasmacytoma: solitary bone (PSO) or intramedullary plasmacytoma and extramedullary plasmacytoma. The bone forms of solitary plasmacytomas are the most frequent.[4, 5, 6, 7]

It is defined as an isolated plasma cell tumor located in a bone segment, which quite often evolves into multiple forms, which calls into question its nosological authenticity for some authors.[8]

The median age at diagnosis is between 55 and 65 years, compared to 71 years for patients with multiple myeloma.[9,10], which corresponds to the median age found in our series. However, PSOs are often diagnosed twice in males than females. Also, cases of solitary bone plasmacytoma have been reported in patients aged 15 years.[11,12] The youngest patient in our sample was 28 years old.

The preferential localization of solitary bone plasmacytomas is the axial skeleton, clinically leading to bone pain and/or neurological disorders by spinal cord compression.[8, 13, 10, 14] In our study, 13 patients had a spinal location followed by 3 cases in the sacrum and all had presented pain.

To make the diagnosis in any case of solitary bone plasmacytoma, a biological assessment is required which includes a blood count with smear, a biochemical examination with calcemia, a renal assessment. Electrophoresis of blood and urine (24 hours) followed by immunofixation to confirm the type of monoclonal immunoglobulin present. Myelogram and bone marrow biopsy are required to confirm solitary bone plasmacytoma or the presence of less than 10% clonal plasma cells. An X-ray workup to assess the extent and severity of the solitary bone plasmacytoma at the time of diagnosis.[6, 7] The biopsy and myelogram had been done in all of our patients.

Radiotherapy is the standard treatment for solitary bone plasmacytoma or associated with surgery (for diagnostic purposes or laminectomy). Irradiation with a recommended dose of 40 to 50 Gy provides a good local control rate of over 90%.[15, 16, 17] They are radiosensitive and radio-curable tumors.[14, 18] In our series, all our patients were treated with radiotherapy with an average dose of 44.02 Gy and 11 cases associated with surgery with good local control (100%).

However, the ideal dose for local control is still imprecise because the dose-effect relationship remains controversial. Some authors have demonstrated the existence of a dose-dependent effect of radiotherapy for better local control. Like Mendenhal et al., They reported a local control rate of 94% with a dose greater than or equal to 40 Gy, against 69% for doses less than 40 Gy.[7]

However, other authors have not found a dose-effect.[19] Thus no dose relationship was found in a study by Tsang et al[20], beyond 35 Gy for small tumors and proposed to reserve high doses for tumors larger than 5 cm. In our series with an average dose of 44.02 Gy, we had a good local control rate. But we cannot conclude that there is a dose-effect given the small number of patients.

The place of surgery in solitary bone plasmacytoma is very limited. It may be indicated for diagnostic purposes, in the event of a neurological complication such as spinal cord compression, or to treat or prevent a pathological fracture in a bone weakened by tumor osteolysis. Complete surgical resection may be indicated in accessible peripheral locations, but it should not be mutilated, given the efficacy equivalent to radiotherapy which, unlike radical surgery, makes it possible to preserve good function.[21,4,22,7] In our series, 11 patients underwent decompressive laminectomy type surgery.

The use of adjuvant or prophylactic chemotherapy for solitary bone plasmacytoma is controversial. Some studies have suggested no benefit from adjuvant therapy[23,17,1], while others have concluded that adjuvant chemotherapy prevents or delays the median time to progression to multiple myeloma.[24, 25]

In a retrospective study of 46 patients with solitary bone plasmacytoma, chemotherapy did not decrease the incidence of transformation to multiple myeloma, but it delayed the median time to progression from 29 to 59 months.[26] A trial of 53 patients with solitary bone plasmacytoma randomized treatment: either local radiotherapy plus melphalan and prednisone for 3 years, or exclusive radiotherapy.[27] After a median follow-up of 8.9 years, disease-free survival was significantly higher in patients treated with radiotherapy and chemotherapy (22 of 25 patients) compared to patients treated only with radiation (13 of 28). It should be noted that there is no high-level evidence showing a benefit of the combination over exclusive radiotherapy for patients with solitary bone plasmacytoma, the decision to give systemic treatment is taken by the doctor oncologist treating and should be individualized based on other important factors such as age, size and location of solitary bone plasmacytoma, local control with definitive radiotherapy, level of monoclonal proteins and molecular or cytogenetic characterization, which may indicate a biologically aggressive disease. In our study, none of our patients received chemotherapy.

The factors predicting local recurrence seem to be, in addition to insufficient doses of radiotherapy, the site of solitary bone plasmacytoma, spinal or pelvic lesions being more difficult to treat than peripheral lesions.[14] Also, tumor size could influence local control. Tsang et

al. had reported a local control rate of 100% in patients with tumors of less than 5 cm against only 38% for larger tumors.[20]

The evolution towards multifocal lesions is a rare and debated situation. It has been described in 2 to 15% of cases in the literature.[14, 10, 28, 2] These are new bone locations at a distance from the first and do not correspond to myeloma dissemination, but a multicentric plasmacytoma. However, its distinction from multiple myeloma is not always easy, especially since a simple bone marrow puncture does not formally exclude dissemination.[29] It was observed in 3 patients in our study with a mean delay of 48.66 months, including 2 patients who had not done spinal MRI. This mode of evolution could be explained by an incomplete diagnostic workup (in particular the absence of exploration by MRI), which leads us to reconsider the diagnosis between a solitary bone plasmacytoma or a solitary plasmacytoma. Moreover, the role of spinal MRI becomes essential in the assessment of solitary bone plasmacytoma, since it has made it possible to correct the diagnosis towards multiple myeloma in a third of cases according to Duarte et al.[30] and Moulopoulos et al.[31] In these two sets of 12 patients each, MRI revealed signal abnormalities in four patients while standard radiographs were normal. The occurrence of myeloma transformation (or multiple myeloma) has been estimated to be 45 to 75%[32], with varying delays of 9 to 130 months.[10, 19] For Maalej et al. the occurrence of multiple myeloma within 24 months casts doubt on the diagnosis of solitary bone plasmacytoma, in which case it could be "occult" myeloma.[18, 33] 5 cases of myelomatous transformation were noted in our study after follow-up without progression at 31 months at 70.8%. The short decline in this series could explain This low rate could be explained by the short decline in our study.

The relationship between solitary bone plasmacytoma and multiple myeloma continues to generate debate in the literature: Are these two distinct entities, or is solitary bone plasmacytoma an early and localized manifestation of multiple myeloma[18]?

The prognosis of solitary bone plasmacytoma remains dominated by the risk of developing multiple myeloma. The factors predicting this myelomatous transformation are multiple. Bataille and Sany, in a compilation of cases from the literature and a personal series of 114 solitary bone plasmacytomas, retained the following 2 factors: age of over 52 years and a vertebral site (vertebral involvement was found in 61.8% of cases of myeloma progression compared to 26.7% in the group of solitary bone plasmacytomas without dissemination).[14] The existence or persistence of a monoclonal peak one year after radiotherapy or after surgical treatment is also a negative factor.[10, 18, 34]

The limited number of these recent studies did not allow definitive conclusions to be drawn. Also in our study, no factor was significantly correlated with progression-free survival (PFS) in univariate or multivariate statistical analysis, probably due to the very small size of our sample.

CONCLUSION

Solitary bone plasmacytoma is a rare malignant tumor whose therapeutic modality of choice is radiotherapy. Our results agree with the data in the literature which confirms that radiotherapy alone is the most effective treatment with better control in more than 90% of cases. However, the size of our series is small to identify the factors predicting transformation into multiple myeloma. Therefore, additional follow-up with a larger series is necessary to demonstrate the correlation between the predictors and the occurrence of multiple myeloma. Which suggests a reflection on the exact place of chemotherapy.

Conflicts of interest

Authors do not declare any conflict of interest.

Authors' contributions

All authors contributed to the writing of this manuscript and approved the final version.

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