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REPORTE DE CASOS

Long-term remission of solitary bone plasmacytoma with minimal marrow involvement treated with only radiation therapy: A case report

Remisión a largo plazo de un plasmacitoma óseo solitario con mínima afectación de la médula tratado solo con radioterapia: Reporte de caso

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Resumen

El plasmacitoma óseo solitario y el plasmacitoma extramedular solitario son entidades raras, caracterizadas por la proliferación localizada de células plasmáticas monoclonales sin afectación sistémica. Hay un estadio intermedio entre el plasmacitoma solitario y el mieloma múltiple (MM) no secretor, conocido como plasmacitoma óseo solitario con mínima afectación de la médula ósea, que tiene un mayor riesgo de progresión a MM.

El porcentaje de infiltración de la médula ósea por células plasmáticas tumorales debe ser inferior al 10 % para que se considere un plasmacitoma óseo solitario con mínima afectación de la médula ósea y no un mieloma múltiple macrofocal no secretor. El presente caso, de un paciente masculino hispano de 42 años de edad, pone de manifiesto la difícil decisión de ofrecer solo una dosis alta de radioterapia frente a una terapia sistémica con trasplante autólogo de médula ósea, dada la infiltración límite del 10 % en la médula ósea. Finalmente, el paciente fue tratado solo con radioterapia, y permaneció libre de progresión tres años después del diagnóstico.

Palabras clave: plasmacitoma, médula ósea, trasplante de médula ósea, mieloma múltiple.

Abstract

Solitary bone plasmacytoma (SBP) and solitary extramedullary plasmacytoma (SEP) are rare entities characterized by localized proliferation of monoclonal plasma cells without systemic involvement. There is an intermediate stage between solitary plasmacytoma (SP) and non-secretory multiple myeloma (NSMM), known as SBP with minimal marrow involvement, which has an increased risk of progression to multiple myeloma (MM).

The percentage of bone marrow infiltration by tumoral plasma cells must be less than 10% to be considered SBP with minimal marrow involvement instead of non-secretory and macro-focal MM. The present case highlights the challenging decision

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Competing interests
The authors declare that they have no competing interests.

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in a 42-year-old Hispanic male patient to offer only high-dose radiation therapy vs. systemic therapy with autologous bone marrow transplantation (ABMT), given the borderline infiltration of 10% in the bone marrow. Eventually, the patient was treated with only radiation therapy, remaining free of progression 3 years after diagnosis.

Keywords: plasmacytoma, bone marrow, bone marrow transplantation, multiple myeloma.

Introduction

The diagnosis of plasma cell neoplasms can be challenging due to the narrow boundaries that may exist between diagnostic criteria (1,2). Solitary plasmacytoma (SP) is a rare disease and corresponds to 5% of all plasma cell neoplasms; it can be subdivided into solitary bone plasmacytoma (SBP) or solitary extramedullary plasmacytoma (SEP) (1,2). As such, SP has an annual incidence of fewer than 450 cases, with an incidence rate reported to be around 0.15/100,000/year (3,4).

There is an intermediate state between SP and multiple myeloma (MM) known as SBP with minimal marrow involvement, which is even rarer and poses a greater challenge both in terms of diagnosis and treatment. Minimal bone marrow disease has been associated with worse outcomes in patients with SP since the presence of clonal plasmacytosis as assessed by immunofluorescence has been associated with a progression-free survival (PFS) of 15 months compared to 42 months for patients without clonal BM involvement (5).

The diagnostic criteria for SBP with minimal marrow involvement require the existence of a tumor composed of plasma cells restricted to a single area of the body and the absence of additional positron emission tomography-computed tomography (PET-CT) lesions; it should not have or only have a minimal monoclonal component, without the SLiM-CRAB criteria, and it is mandatory to have less than 10% of bone marrow involvement (2,4,6).

Here we present the case of a male patient with SBP of the spine with exactly 10% infiltration in bone marrow biopsy, debuting with cord compression syndrome, and no monoclonal component identified in blood and urine. As mentioned before, since the level of bone marrow infiltration was 10%, the challenge was to classify the disease either as non-secretory and macro-focal MM and offer standard induction treatment, high doses of chemotherapy, and maintenance, or SBP with minimal marrow involvement and treat him only with radiation therapy.

Eventually, the patient was only treated with radiation therapy with curative intent. At present, the patient has a PFS of more than 36 months, recovering his functionality to 100% without using systemic treatment.

Clinical case

We present the case of a 42-year-old Hispanic male patient with an Eastern Cooperative Oncology Group (ECOG) performance score of 0 and unremarkable past medical history, who presented initially with constitutional symptoms, mainly with a 10 kg weight loss in 6 months, low back pain with paresthesia, and progressive loss of strength in his right leg until complete compromise of mobility at this level. Spinal magnetic resonance imaging (MRI) showed an infiltrative process of the lumbosacral spine vertebrae with destruction of the intervertebral discs, edema, and irregularity of the adjacent vertebral endplates in L2-L3 and L5-S1. PET-CT showed no additional lesions in any body segment (see figure 1 for baseline PET-CT).

A discectomy plus hemilaminectomy was performed, with vertebral body biopsy of L2-L3 and L5-S1 showing tumor cells expressing CD38 and CD138, with negative CD56, and without light chain restriction. The bone marrow study revealed exactly 10% infiltration with CD38 immunophenotype tumoral plasma cells (figure 2).

Protein study showed non-measurable monoclonal component both in blood and urine (figure 3). Hemoglobin, calcium, and creatinine levels were normal, as well as the kappa and lambda ratio.

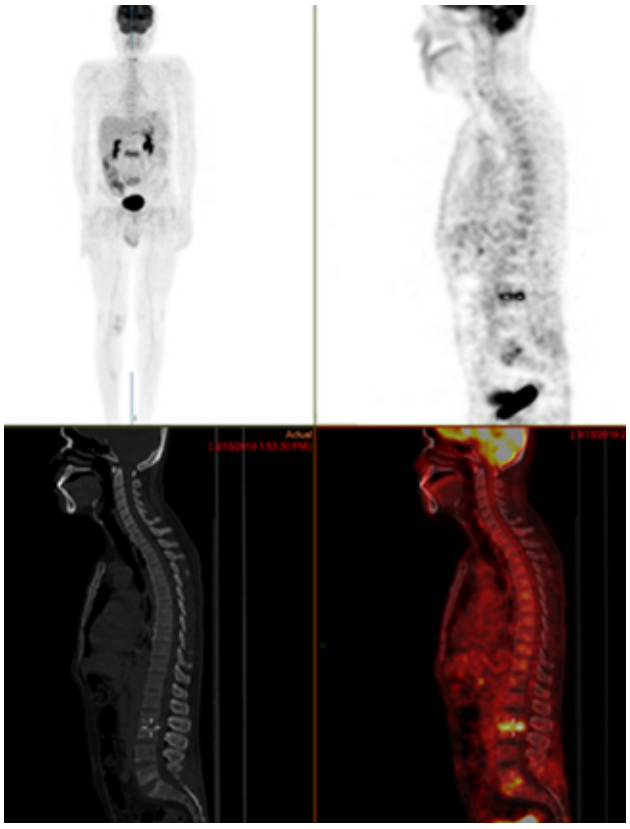


Figure 1. Baseline PET-CT showing two intense uptake foci in the lumbar spine at intervertebral spaces L2-L3 and L5-S1, with tumor activity due to plasmacytoma in 18F-FDG PET-CT. **Upper right view:** Sagittal PET. **Upper left view:** Maximum intensity projection. **Lower right view:** Fused sagittal image. **Lower left view:** Sagittal CT.

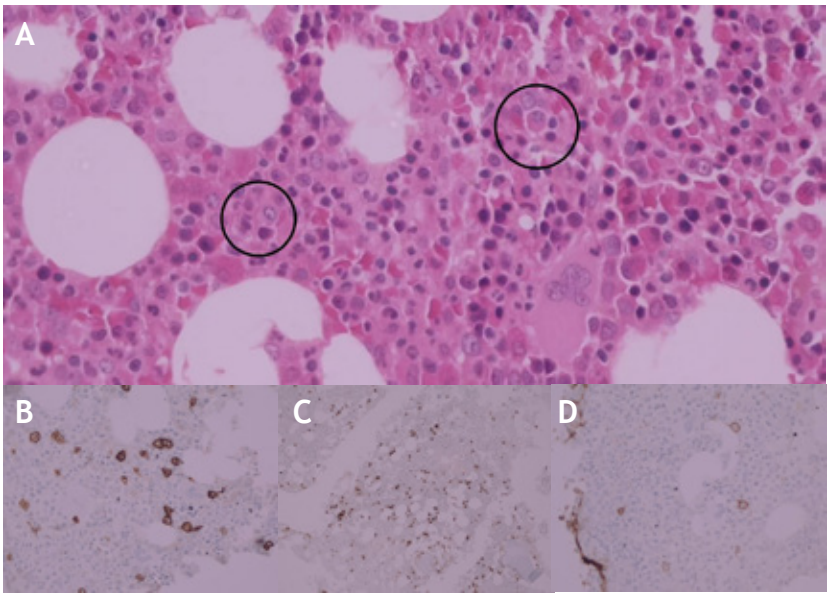
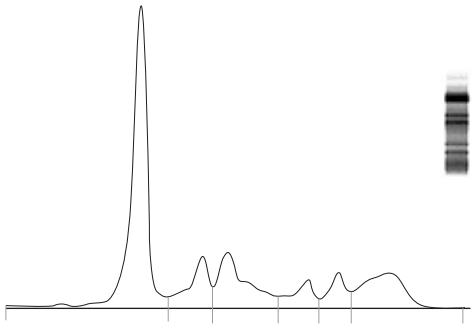


Figure 2. Immunohistochemistry. **A.** Immunohistochemistry showing 10% bone marrow infiltration, hematopoiesis of all three lines, and few plasma cells. **B.** Immunohistochemistry for CD38, 40x; positivity of plasma cells with abnormal morphology. **C.** Immunohistochemistry for CD 138, 10x; positivity of plasma cells. **D.** Cells with abnormal morphology.



Axis x: Serum protein electrophoresis

Fractions	%		Ref. %	Conc.	Ref. Conc.
Albumin	46.5	<	55.8 - 66.1	3.3	4.0 - 4.8
Alpha-1	10.1	>	2.9 - 4.9	0.7	0.2 - 0.4
Alpha-2	16.2	<	7.1 - 11.8	1.2	0.5 - 0.9
Beta 1	5.9		4.7 - 7.2	0.4	0.3 - 0.5
Beta 2	6.1		3.2 - 6.5	0.4	0.2 - 0.5
Gamma	15.2		11.1 - 18.8	1.1	0.8 - 1.4

T.P.:**7.1** g/dl

A/G Ratio: **0.87**

A/G Ratio: Albumin/globulin ratio; Conc.: Concentration; Ref. Conc.: Reference concentration; Ref. %: Reference percentage; T.P.: Total protein.

Figure 3. Serum protein electrophoresis with moderate increase in the alpha-1 and alpha-2 regions, mild hypergammaglobulinemia, but no monoclonal component and negative immunofixation.

A diagnosis of SBP with minimal marrow involvement of the spine vs. non-secretory and macro-focal MM was proposed. We decided to diagnose him as SBP with minimal marrow involvement regardless of borderline 10% of bone marrow infiltration. The patient was treated with 50 Gy of local radiation therapy with curative intent, without any chemotherapy or bone marrow transplantation. After radiation therapy, the patient was considered to have a complete response, with the resolution of basal lesions on imaging and complete recovery of neurologic function. The patient has evolved satisfactorily with clinical betterment and progressive improvement in muscle strength. At 3-year follow-up, the patient is doing well without disease recurrence or constitutional symptoms, and he is free of neurological manifestations.

Discussion

Plasma cell neoplasms often represent a significant challenge in terms of diagnosis and treatment due to the narrow boundaries that may exist between diagnostic criteria and multiple options for treatment (1,2,7). Most of the time, the criteria for diagnosing MM and related diseases help homogenize the characteristics of patients to be included in clinical trials rather than define the appropriate therapies in real-life clinical practice (8).

There are several types of plasma cell neoplasms. These diseases are almost always associated with a monoclonal protein (M-protein), and not too often, there can be non-secretory diseases.They include monoclonal gammopathy of undetermined significance (MGUS), amyloidosis, POEMS syndrome, SBP, SEP, latent MM, macro-focal MM, symptomatic MM, and plasma cell leukemia (1,9).

SP is considered a rare disease characterized by localized proliferation of monoclonal plasma cells; frequently, its main symptom is pain localized in the thoracic and lumbar spine zone. This neoplasm can be subdivided into SBP or SEP (1,2).

Diagnostic criteria for SBP with minimal marrow involvement include 1) a solitary lesion identified by MRI and confirmed by biopsy, with infiltration of plasma clonal cells; 2) absence of organ damage related to myeloma (anemia, hypercalcemia, renal failure, hyper-viscosity, amyloidosis, bone damage, or recurrent infections); 3) plasma cells that constitute less than 10% of the nucleated cells of the bone marrow; and 4) absence of M-protein in urine or serum (2-5).

Our patient fulfilled all these criteria; however, the level of bone marrow infiltration was exactly 10%. As SBP tumors are sensitive to radiation, it is the treatment of choice to eradicate local lesions in most cases, even when there is minimal marrow involvement. Local control is achieved with radiation therapy, and in some circumstances, it can be a curative option by itself. Initial trials have demonstrated response rates as high as 92% in SBP patients who received local radiation therapy.

In a retrospective study, the 5-year progression rate was 47%, being higher in patients with SBP than with SEP (56% vs. 30%) (10).

It is important to note also that patients with minimal marrow involvement are at higher risk for progression to MM than those cases with no detectable plasmacytosis in the marrow. This was demonstrated in a retrospective review of 127 patients at the Mayo Clinic, which showed that patients with plasmacytoma and detectable clonal plasma cells in the marrow were at much higher risk for progression and even death. The median PFS was 42 months in patients with negative bone marrow involvement compared to 15 months in patients with detected clonal plasmacytosis (2,3,5).

The current recommended dose and schedule is fractionated radiation therapy at a total dose of 40-50 Gy over 4 to 5 weeks in daily doses. The treatment field should cover all tissues identified by imaging; that was the treatment we used in our patient, who remains in remission at present (3,4).

In tumors with poor prognosis, guidelines recommend using adjuvant chemotherapy and reserving surgery for complications such as spinal or root compression or vertebral collapse. If surgery is necessary, so it will be the use of radiation therapy (3,6).

The utility of chemotherapy in SBP and SEP has been studied, but, unfortunately, there has been insufficient data to recommend it to improve disease control or prevent progression to MM following radiation. An earlier retrospective study of 46 patients with SBP and SEP showed that adjuvant chemotherapy did not affect the rate of progression to MM, as 64% of patients receiving chemotherapy still progressed (11).

Despite good disease control following the initial treatment, in a third of patients, the disease could eventually evolve to generalized myeloma or add solitary or multiple plasmacytomas in approximately 10 years, sometimes due to the presence of a hidden generalized disease. One study demonstrated that at 5 years, more than 50% of patients had relapsed, and the median time to develop MM was 21 months (12). It seems that cytogenetic and molecular assessment could improve to define the risk of progression in these patients (13).

It is important to continue close surveillance to detect a possible early relapse in the patient. The presented case demonstrates that we have excellent strategies to offer to our patient since he has not been exposed to chemotherapy regimens (2,7,14).

Conclusions

Given the rarity of this case and the positive response rate to the identified treatment, we believe that the impact of communicating these findings can be outcome-changing.

Declarations

Ethics approval and consent for publication

Our manuscript does not report on an investigational therapy, nor does it involve the use of any animal or human data or tissue in experiment; hence, this section related to ethics approval does not apply to our submission. The use of data was approved by the Research Ethics Committee of the *Instituto Nacional de Cancerología* (Bogotá, Colombia), in a meeting held on March 17, 2021.

Consent for publication

Written informed consent was obtained from the patient for the publication of this case report and any accompanying imaging.

Availability of data and materials

Data are available on request.

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Authors' contributions

HMC analyzed and interpreted the patient's data regarding the hematological disease and treatment of choice and contributed to writing the manuscript. DSB performed the literature search and contributed to writing the manuscript. SCP analyzed and interpreted the patient's PET-CT and contributed to writing the manuscript. All authors have read and approved the final manuscript.

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