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CASE REPORT

Radiation response of soft-tissue extramedullary plasmacytoma in multiple myeloma—A case report

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Abstract

We report the case of a 79-year-old female patient previously treated for multiple myeloma that was referred to our hospital due to a growing painless right arm tumor. Imaging and pathology results confirmed the diagnosis of extramedullary plasmacytoma. The patient underwent external beam radiotherapy with complete clinical response at follow-up.

KEYWORDS

complete response, multiple myeloma, radiotherapy, soft-tissue plasmacytoma

1 | INTRODUCTION

Plasmacytoma is a frequent complication of multiple myeloma (MM), and it can be found either at diagnosis or within disease progression. It is defined as a tumor mass composed of aberrant plasma cells. Plasmacytoid lymphocytes and plasma cells are small- to medium-sized cells that are also found in body fluids and in the spleen.[1] Previously reported studies show that irradiation can produce toxicity on plasmacytoid lymphocytes and plasma cells as was also shown in unintentional irradiation toxicity on lymphocytes count in spleen volume (spleen).[2] Plasmacytomas can be isolated, with no other evidence of MM, in which case they are known as solitary plasmacytomas (solitary plasmacytoma of the bone and solitary extramedullary plasmacytoma), although more frequently they occur during the course of the disease.[3] Extramedullary plasmacytomas (EMP) account for almost 7 to 18 percent of patients with MM at diagnosis.[4] An extremely small number of MM patients might develop soft-tissue EMP, which may constitute a more prominent clinical feature, and although most soft-tissue tumors arise as direct extensions from skeletal tumors when they disrupt the cortical bone, that is not always the case.[5] We present a case of a female MM patient that developed soft-tissue EMP in the arm, which was treated by external beam radiotherapy

(EBRT) with curative intent and presented at follow-up with complete clinical remission.

2 | CASE HISTORY

A 79-year-old female patient presented at "Prof. Dr. Alexandru Trestioreanu" Oncology Institute from Bucharest with acute pain, limiting functionality, and swelling of the right arm which started 3 weeks prior to hospital admission. On scrutiny of patient's medical history, it resulted that she was previously diagnosed with thoraco-cervical vertebral MM two years before. The patient underwent bortezomib-cyclophosphamide-dexamethasone (VCD) chemotherapy protocol for up to 8 cycles, every 21 days (q3w), concurrently with zoledronic acid. The treatment was well tolerated with minimal side effects. At the last chemotherapy cycle, the patient presented with right arm swelling; therefore following the last chemotherapy cycle, full-body CT scan was performed indicating complete clinical remission of thoraco-cervical vertebrae tumoral mass, but with a new tumor mass developing in the right arm connective tissue with no signs of humerus invasion. The patient was further referred to our hospital for supplementary investigations and treatment.

3 | INVESTIGATIONS AND TREATMENT

At presentation, the patient had (Figure 1A) painful (level 8—Visual Analogue Scale) right arm swelling, limited functionality, telangiectasia and superficial, dilated, vertically oriented and tortuous cutaneous venules; therefore, initially, a soft-tissue ultrasound was performed, revealing a 10/6.2/9.5 cm intramuscular mass with extension in the surrounding adipose tissue. Subsequently, an ultrasound-guided biopsy was taken. The pathology and immunohistochemistry (Figure 2) examinations indicated connective tissue encompassing groups of plasma cells with a plasma cell appearance, plasma positive tumor proliferation, positive for MUM1 (multiple oncogenic myeloma 1) with clonal character (kappa/lambda—20/1), negative for CD56. Following these results, bone marrow biopsy was taken revealing a hypercellular hematogenous marrow (90% cellular component) by diffuse infiltration > 80%, dislocation of normal hematopoiesis, plasma cell type medullary infiltration, diffuse CD138 positive and CD20 negative. This type appearance was compatible with a medullary infiltration > 80% of multiple plasma cell myeloma. Electrophoresis was performed, obtaining the following results: light kappa type chains—38 mg/L (3.3–19.4), serum lambda free chains—11.9 (5.7–26.3), and kappa/lambda ratio—3.19 (0.26–1.65). All these data resulting from the pathological and immunohistochemistry examinations confirmed the diagnosis of extraosseous plasmocytic plasmacytoma with secretion of light kappa chains as a result of MM. At a right arm magnetic resonance imaging (MRI), an expansive tumor was identified (Figure 3A), with both humeral erosion and extension in the adjacent adipose muscle tissues measuring axially about 11.6/8.2 cm and craniocaudally about 13.2 cm, with diffuse edematous infiltration of the adjacent cellulo-adipose tissues, without definite interruption of the straight humeral bone cortex. After case evaluation in the rare tumors multidisciplinary board, the

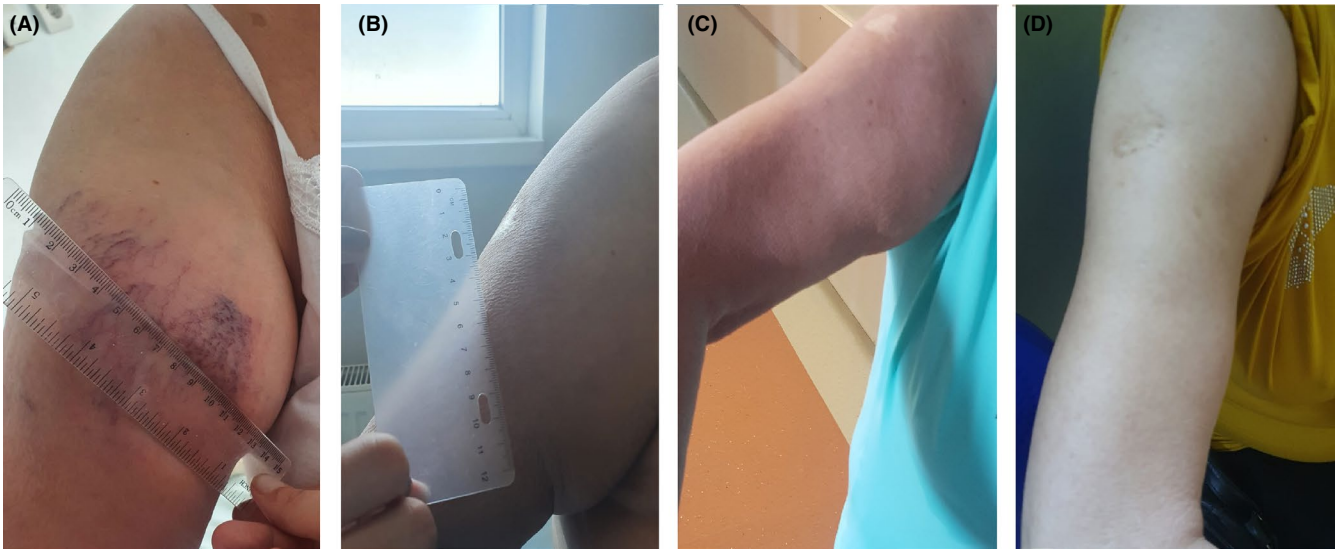

FIGURE 1 Right arm tumor and associated clinical signs at presentation (A), during external beam radiotherapy (after 30 Gy – B and at the end of the treatment at 45 Gy – C) and at follow-up (D)

decision was for radiotherapy with palliative intent. In the upcoming weeks, the patient underwent EBRT using 3D conformal technique up to a total dose of 30 Gy using a daily 3 Gy fractionation schedule. Due to clinically significant improvement in arm mobility and tumoral decrease (Figure 1B), the treatment was continued up to a total dose of 45 Gy, using the same fractionation schedule. All treatment sessions were done using an upper-body Vac-Lok cushion with the patient supine and right upper arm Akimbo positioned. Initially, opioid analgetic and anti-inflammatory medication was used. The treatment was well tolerated and with good clinical response and at the end of the treatment the patient presented with complete pain relief without needing analgetic medication, tumor reduction and regained arm mobility with grade 2 local radiation dermatitis (Figure 1C).

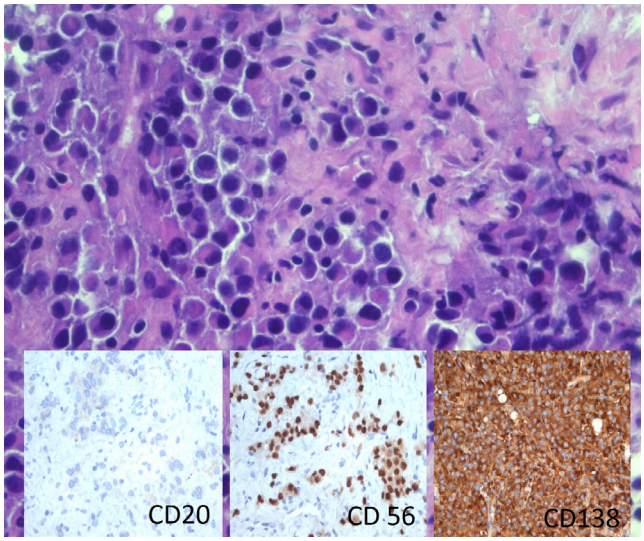

FIGURE 2 Extramedullary plasmacytoma pathology and immunohistochemistry results. The tumor was positive for CD138 plasma cell marker, negative for CD20 and showed loss of expression for CD56

4 | OUTCOME AND FOLLOW-UP

Three months later, at follow-up, the patient presented no signs of clinical tumor relapse, with complete recovery of arm mobility and no therapeutic side effects (Figure 1D). Six months following treatment end, the right arm and glenohumeral joint MRI describe complete tumoral remission with complex changes of form and structure at the level of the straight humeral proximal metaphyseal-diaphyseal region that associate osteoid changes (Figure 3B). Imaging report describes spongy tissue signal displaced by masses with heterogenous hypersignal, with thinning of the bone compact in the injured region, with intermittent hypersignals at the level of the adjacent muscle planes. Also, similar signal changes are described in the acromio-clavicular

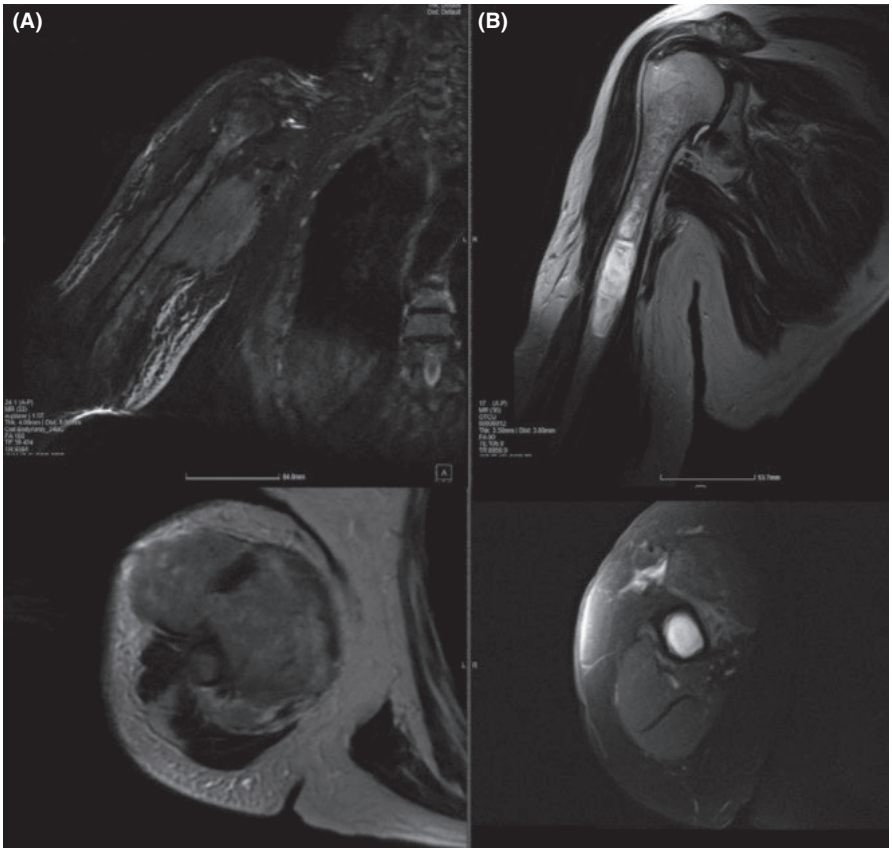

FIGURE 3 Magnetic Resonance Imaging axial and coronal view T2 short tau inversion recovery (STIR) images from diagnosis (A) and six months following treatment (B)

joint. The patient's clinical condition and imaging showed a favorable evolution at the 3 months follow-up. The intent is to reassess her status clinically at every 3 months, and at every 6 months with imagistic investigations such as MRIs and routine blood tests.

5 | DISCUSSION

Soft-tissue plasmacytomas in MM can have two different origins: direct extension from skeletal tumors, when they disrupt the cortical bone, or hematogenous metastatic spread.[6] In the setting of MM, EMP has a poor prognosis, with a median overall survival ranging from 4 to 12 months according to bone infiltration.[7] Although hematogenous metastatic spread occurs more frequently in the skin, liver, kidney, or central nervous system, in our patient the tumor was soft tissue located, which it is suggested to be linked to extension from a skeletal tumor.[8] Recent epidemiological studies[9] have shown a statistically significant increase of EMP involvement in the last decade, and this was due to an increase in detection rates. Modern imaging and immunohistochemical tumor characteristics were found to be responsible for this. In recent years, using high-performance imaging techniques, such as MRI and PET-CT on a larger scale and including them in the follow-up guidelines for MM patients has led to an increase in the detection rate of EMP.[10] Following that, bone scan and bone marrow biopsy should also be performed in order to find the relationship with the primary diagnosis,[11] in this case MM. For our patient, right arm MRI revealed homogeneous low signal intensity on T1-weighted images and high signal on T2-weighted images. Alongside the MRI and immunohistochemistry reports, bone scan and bone marrow biopsy data confirmed the EMP diagnosis and its emergence from MM. Regarding the immunohistochemical profile of the tumor, previously published data[12] suggest that EMP have similar immunophenotypic abnormalities to those encountered in standard MM. The loss of expression of CD56 was used to differentiate the tumor from solitary lymphoma lesion, and it is also considered one unfavorable prognostic factor, being associated with hematogenous metastatic spread and decreased OS in EMP and MM patients.[4,13] Considering this and the results from Santiago et al.,[14] our patient's immunohistochemistry data showed CD56 loss of expression, with CD138-positive and CD20-negative results confirming the diagnosis of EMP. As for the treatment of EMP, a local approach is considered the most suitable and with increased chances of success rate. Unlike in other radioresistant tumors (eg, cervix uteri, colorectal)[15,16] that showed unpredictable radiation response, for plasmacytoma previously published data showed a more favorable outcome even at lower radiation doses. Therefore, surgery or local radiotherapy have been associated with encouraging results in previously published studies[17] leading to high 10 years local control (>70%) and OS (>50%) survival rates. For our patient, due to factors such as age, tumor size, and surgical side effects, and also considering the increased radiosensitivity of EMPs, a limb sparring therapeutic approach was recommended by the multidisciplinary team, that is why radiotherapy was proposed. Initially, radiotherapy was administered up to a palliative dose 30 Gy, considered safe and effective based on published data[18] using a 3 Gy fractionation schedule, but due to increased clinical outcomes, treatment was continued, boosting it up to a total dose of 45 Gy, according to SoutarR.et al.[19] recommendations, with the same fractionation schedule, in order to obtain longer local tumor and symptom control and also a potential curative response.

6 | CONCLUSION

Extramedullary plasmacytoma is a rare and aggressive tumor, associated with a poor prognosis when it is linked to or develops concomitant to MM. We presented the case of a patient, already known with MM, treated by chemotherapy and with a complete clinical response following treatment that developed an EMP of the right arm. Considering tumor radiosensitivity and multidisciplinary board decision, the patient underwent palliative radiotherapy up to 30 Gy and boosted up to 45 Gy due to clinical tumor response. Six months following treatment cessation, the patient showed no signs of tumor relapse and maintained clinical response. Adapting radiotherapy dose according to tumor size and intratherapeutic tumor response proved to be of great success in disease control. However, controlled clinical trials are necessary to establish a definitive treatment of choice. Also, regarding follow-up, a lifelong evaluation for disease progression is necessary with all plasmacytomas.

ACKNOWLEGEMENTS

None.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

Alexandra Gaube and Silvia Gabriela Nica involved in literature research and manuscript writing. Filip Stefan Calangiu involved in critical feedback and manuscript revisions. Camelia Dobrea and Stefania Ariana Neicu involved in pathology examination and description, and

literature review. Vanessa Gabriela Moldoveanu involved in language and manuscript editing. Magda Serbanescu involved in imaging description and literature review.

CONSENT

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

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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