Extramedullary Disease of the Breast in Multiple Myeloma—An Uncommon Initial Presentation: A Case Report and Review of Literature

Priyadarshini Venkataraman[1] Nikitha Mehra[2] Shirley Sundersingh[3] Priya Iyer[1]

[1] Department of Radiation Oncology, Cancer Institute WIA Adyar, Chennai, Tamil Nadu, India
[2] Department of Medical Oncology, Cancer Institute WIA Adyar Chennai, Tamil Nadu, India
[3] Department of Oncopathology, Cancer Institute WIA Adyar Chennai, Tamil Nadu, India

Address for correspondence Priyadarshini Venkataraman, MD, Department of Radiation Oncology, Cancer Institute WIA Adyar, Chennai 600022, Tamil Nadu, India (e-mail: Priya.venkat@yahoo.com).

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Abstract

Multiple myeloma (MM) is a malignancy characterized by the abnormal proliferation of plasma cells within the bone marrow. It is typically defined by the presence of $\geq$10% clonal bone marrow plasma cells and is associated with hypercalcemia, renal failure, anemia, or lytic bone lesions. Extramedullary disease (EMD) in MM, where plasma cells proliferate outside the bone marrow, is rare. While several case reports on the solitary plasmacytoma of the breast have been reported in the literature, EMD in the breast as an initial presentation of MM is exceedingly rare. We report the case of a 32-year-old female who initially presented to the outpatient department with a lump in her left breast, persisting for 2 months, with no other associated symptoms. Upon evaluation, she was diagnosed with MM International Staging System stage II EMD. The patient underwent standard treatment along with consolidative radiation therapy targeting the breast mass. She achieved a very good partial response (VGPR) and remains in VGPR. Given the rarity of EMD as an initial presentation in MM, the role of radiation therapy in its management remains unclear. In this case report, we utilized radiation therapy as a consolidative treatment with a suitable outcome.

Keywords
- breast
- extramedullary disease
- multiple myeloma
- radiation therapy

Introduction

Plasma cell neoplasms constitute a spectrum of disorders, including monoclonal gammopathy of unknown significance, smoldering multiple myeloma (MM), solitary plasmacytoma, MM, and plasma cell leukemia. MM represents 1% of all cancers and 10 to 15% of hematological malignancies globally.[1,2] Extramedullary disease (EMD) in MM is the proliferation of plasma cells beyond the confines of the bone marrow. It can be present at diagnosis (primary) or occur as a relapse (secondary).[3,4] The incidence of primary EMD is 4 to 16%, and secondary EMD is 6 to 20% during the progression of MM.[5] Here we report an atypical manifestation of primary EMD of the breast at presentation in a case of MM.

Case Report

We report a 32-year-old premenopausal female with no significant family history. She presented with a lump in her left breast of 2 months duration. Clinical examination revealed a tumor measuring 12 $\times$ 12 cm, occupying the entire left breast with impending ulceration in the lower

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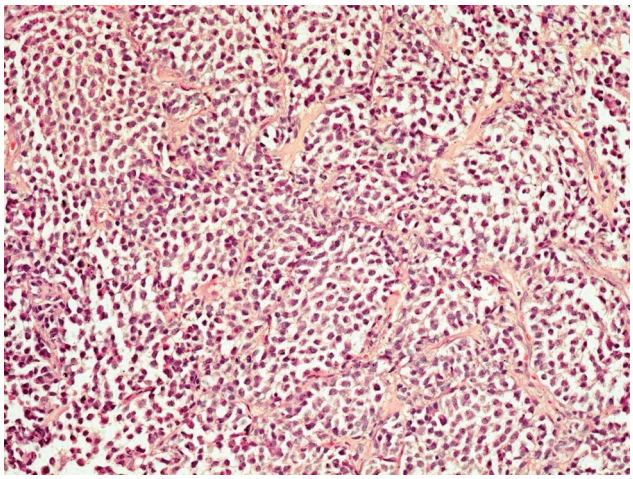

Fig. 1 Sheets of neoplastic plasma cells including binucleate forms. H&E 200×.

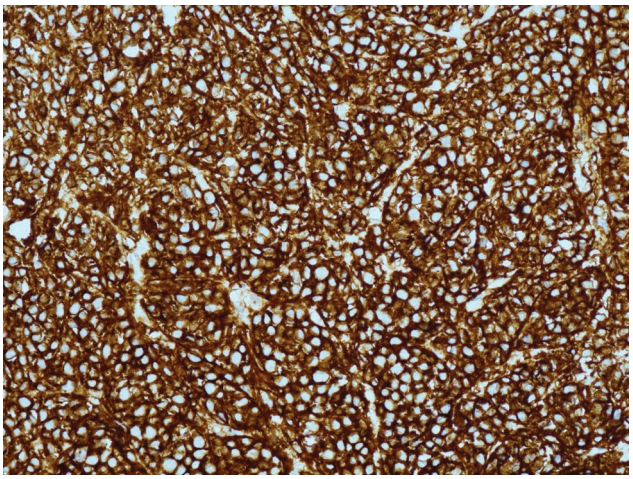

Fig. 3 Neoplastic plasma cells positive for CD138. DAB 200×.

quadrant. The presentation also included peau d'orange, affecting all quadrants of the breast. An enlarged, firm lymph node of size 2 × 1 cm was noted in the left axilla. The right breast and axilla were normal, and other staging workups revealed no distant metastasis. A core biopsy, with immunohistochemistry (IHC) correlation, suggested a plasma cell neoplasm. The atypical cells were positive for CD138, Mum-1, CD20 and Lambda, and negative for Kappa with a Ki 67 of 80% and a mitosis of 2/high power field (►**Figs. 1**–**7**).

We initiated a myeloma workup, which revealed an M protein level of 2.3 g/dL by serum electrophoresis, IgG Lambda type on serum immunofixation electrophoresis, a serum kappa and lambda ratio of 0.12 (kappa: 9.4 mg/L, lambda: 76.5 mg/L), a bone marrow biopsy suggestive of plasma cell neoplasm, and a bone marrow aspiration revealing 62% plasma cells. A whole-body 18-fluorodeoxyglucose positron emission tomography (FDG-PET) scan indicated a 7.2 × 8.5 × 10 cm soft tissue mass with necrotic areas in all quadrants of the left breast, infiltrating the skin with an SUVmax of 9.18 (►**Fig. 8**). Enlarged left axillary lymph nodes measuring 2 × 1 cm with an SUVmax of 2.27 were also observed, with no evidence of disease elsewhere. She was diagnosed with MM International Staging System (ISS) stage II EMD.[6] Cytogenetic analysis by interphase fluorescence in situ hybridization was not performed.

The patient received six cycles of lenalidomide, bortezomib, and dexamethasone chemotherapy, with monthly injections of zoledronic acid 4 mg. She achieved very good partial response (VGPR). The patient then underwent autologous stem cell transplant (ASCT). Post-ASCT, she was planned for consolidation radiation therapy to the residual breast disease to a total dose of 42.5 Gy at 266 cGy per fraction over 16 days. After completion of radiation, she received three cycles of consolidation chemotherapy followed by maintenance lenalidomide. The patient remains in VGPR.

Discussion

Extramedullary plasmacytomas (EMPs) can occur in various organs, including the skin, lungs, gastrointestinal tract, bladder, head, and neck.[7] Breast plasmacytoma (BP)

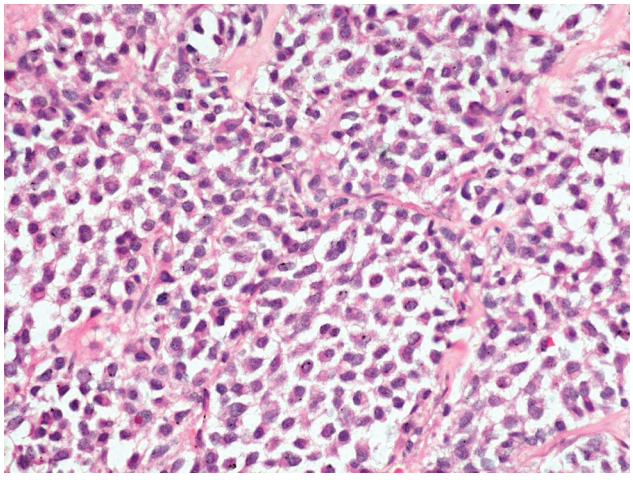

Fig. 2 Sheets of neoplastic plasma cells including binucleate forms. H&E 400×.

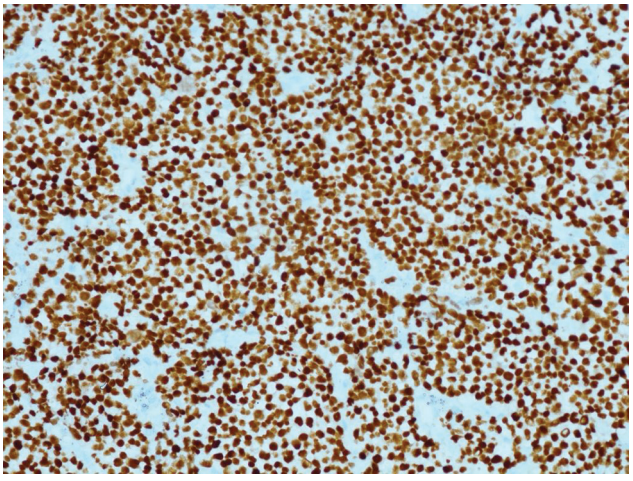

Fig. 4 Neoplastic plasma cells positive for Mum 1. DAB 200×.

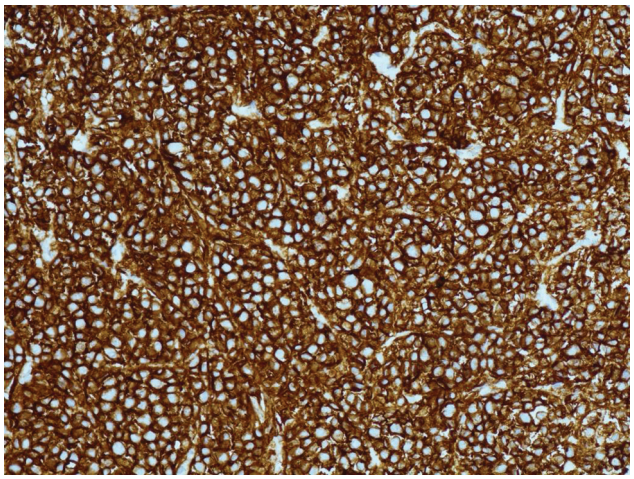

Fig. 5 Neoplastic plasma cells positive for CD20. DAB 200×.

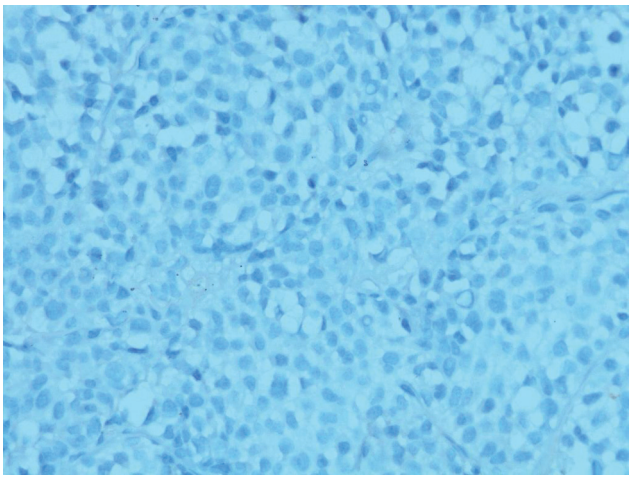

Fig. 7 Neoplastic plasma cells negative for Kappa. DAB 200×.

represents 1.5% of all plasmacytoma cases. Among these, 15% are categorized as primary BP, while the remaining cases are secondary events associated with MM.[8,9] The occurrence of plasmacytoma in the breast, either as an isolated EMD or as a manifestation of widespread MM, is infrequent. Very few cases have been reported to date.[8,10,11] Variability in the occurrence and prevalence of EMD in MM complicates the approaches to diagnosis and management. A tumor biopsy with IHC confirms EMD, followed by routine myeloma investigations. Imaging includes PET-computed tomography (PET-CT) to evaluate the extent of the disease.[12–15] EMD in MM is an unfavorable prognostic factor,[16,17] although it is not included in the conventional ISS and R-ISS (revised-ISS) staging systems.[18]

Our patient presented with a large breast tumor that was clinically and radiologically indistinguishable from a solid breast tumor, even with mammography. Given the rarity of this condition and the absence of other symptoms, diagnosing MM was highly challenging. Histopathological analysis was the only method that confirmed the breast lump as MM, which subsequently led to further investigations, including a PET-CT scan and bone marrow biopsy. As our patient was transplant-eligible and completed the protocol treatment as planned, we considered radiation therapy as a consolidative treatment. This approach yielded a favorable response, suggesting that radiation could be a viable option for similar cases. Recommendations propose doses up to 50 Gy in 25 fractions for solitary bone plasmacytomas and solitary EMPs larger than 5 cm.[19–21] For plasmacytomas measuring 5 cm or less in size, suggested doses are approximately 40 Gy in 20 fractions.[19,20] In this case, the size of the tumor was more than 5 cm, so we considered a total dose of 42.5 Gy at 266 cGy per fraction with a biological effective dose of 79.3 Gy and an equivalent dose in 2 Gy (EQD2) of 47.6 Gy to the whole breast including the residual tumor.

The management of EMD with MM includes induction chemotherapy and ASCT in transplant-eligible patients, followed by consolidation and maintenance therapy.[22,23]

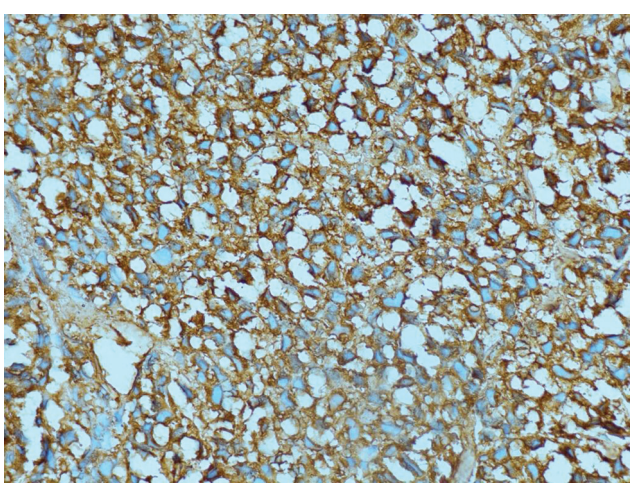

Fig. 6 Neoplastic plasma cells positive for Lambda. DAB 200×.

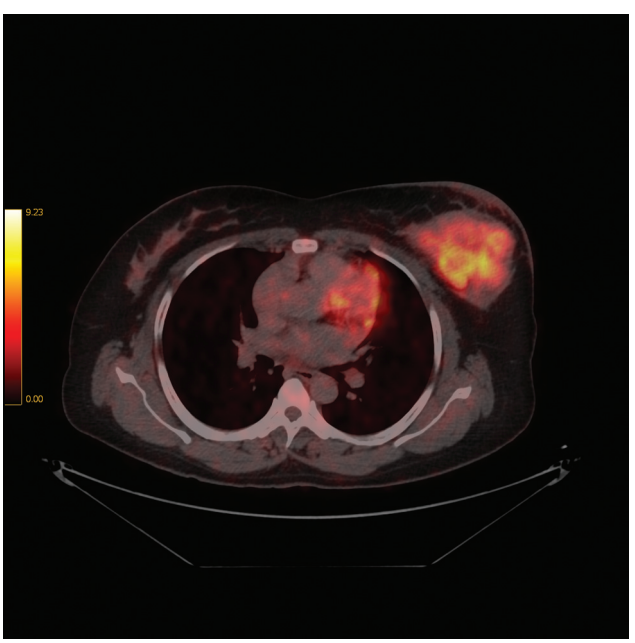

Fig. 8 PET CT showing soft tissue mass with necrotic areas in the left breast. CT, computed tomography; PET, positron emission tomography.

Surgery has often been used as a local treatment, but the use of radiation therapy has been exceedingly rare. In the management of MM, radiation is utilized for treating EMD, pain palliation, and prophylactic therapy for impending fractures.[24] It has demonstrated remarkable efficacy in achieving local disease control in solitary osseous and extraosseous plasmacytoma.[19,20,25] Various aspects, such as the optimal radiation dosage, radiation fields, fractionation, etc., still need to be determined.

Conclusion

The features of MM in the breast closely imitate those of other breast diseases, whether originating within the breast or spreading from different locations. This underscores the importance of considering such rare presentations in the differential diagnosis. With appropriate histopathological analysis, an accurate diagnosis can be achieved. This case report highlights the value of a multi-modality treatment approach, which led to a favorable outcome in our patient, who continues to maintain a VGPR. However, due to the limited availability of prospective studies, it is challenging to strongly advocate for a specific treatment approach. The role of radiation therapy in such cases remains unclear and requires further research to determine the optimal dose fractionation and total dose.

Note

We hereby confirm that the manuscript has been read and approved by all the authors. Each author has met the criteria for authorship as defined by the journal's guidelines, and we collectively affirm that the manuscript represents honest and original work.

Patient's Consent

Patient consent has been obtained.

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Conflict of Interest

None declared.

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Contribution details

	Contributor 1	Contributor 2	Contributor 3	Contributor 4
Concepts	✓			✓
Design	✓			✓
Definition of intellectual content	✓	✓	✓	✓
Literature search	✓			
Clinical studies				
Experimental studies				
Data acquisition				
Data analysis				
Statistical analysis				
Manuscript preparation	✓			✓
Manuscript editing	✓	✓	✓	✓
Manuscript review	✓	✓	✓	✓

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