CASE REPORT

DOI: 10.5336/caserep.2025-111284

Presentation of Multiple Myeloma with Extramedullary Plasmacytoma After Autologous Stem Cell Transplantation

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This study was presented as a summary orally in 5th Congress on Stem Cells and Cellular Therapies in April 19-20, 2024, İstanbul, Türkiye.

ABSTRACT Plasmacytoma is a type of plasma cell neoplasm that can occur as either solitary bone plasmacytoma or extramedullary plasmacytoma (EMP). EMP occurs in 8-31% of multiple myeloma (MM) cases and usually affects the upper respiratory tract. We report the case of a 67-year-old woman with MM who developed nodular skin lesions on her head, abdomen, and the middle finger of her right hand 2 months after autologous stem cell transplantation. A skin biopsy confirmed cutaneous EMP. Positron emission tomography and computed tomography imaging showed no systemic or extracutaneous involvement. The patient was started on daratumumab, lenalidomide, and dexamethasone. Radiotherapy was initiated because the existing skin lesions did not improve and caused pain. After 8 months of treatment, new lesions appeared, leading to the discontinuation of lenalidomide and a switch to daratumumab-pomalidomide-dexamethasone. Despite systemic therapies such as chemotherapy and immunotherapy, the prognosis remained poor. This case report contributes to the limited literature on post-transplant cutaneous EMP and emphasizes the importance of multidisciplinary management in complex MM cases.

Keywords: Plasmacytoma; multiple myeloma; stem cell transplantation

Plasmacytoma is a neoplasm composed of neoplastic plasma cells and typically involves only one area. Although it can develop in multiple organs and tissues associated with multiple myeloma (MM), it can also occur independently as a primary form, called solitary plasmacytoma. Solitary plasmacytoma does not have the systemic features of MM.[1] It has 2 main clinical types: solitary bone plasmacytoma and extramedullary plasmacytoma (EMP). Although EMP occurs 3 times more often in males than females, it makes up 3-5% of all plasma cell disorders. EMP has been reported to turn into MM in 8-31% of cases, mostly in the head and neck, often affecting the submucosa of the paranasal sinuses, nasal cavity, nasopharynx, and tonsils.[1] Rarely, it can appear in the skin, gastrointestinal tract, lungs, or limbs.[2] Cutaneous EMP is especially rare, accounting for less than 1% of all EMP cases, and is usually linked to advanced or recurring MM. Its presentation as subcutaneous nodules or plaques creates diagnostic challenges because of its nonspecific appearance, often resembling other skin conditions such as cutaneous lymphoma or metastatic cancer. Recognizing cutaneous EMP early is important, as it often indicates aggressive disease and a poor outlook.[4,5]

Differentiating EMP from MM involves the presence of one or more EMPs, normal and nonclonal plasma cell morphology in bone marrow aspi-

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Peer review under responsibility of Turkiye Klinikleri Journal of Case Reports.

Received: 15 Apr 2025 ***Accepted:*** 09 Sep 2025 ***Available online:*** 30 Sep 2025

rate biopsy samples, the absence of osteolysis, hypercalcemia, or renal failure, and the lack of M-protein in protein electrophoresis and serum/urine immunoelectrophoresis. EMP is commonly assessed using histological markers such as CD38, CD138, kappa light chains (KLC), lambda light chains (LLC), CD20, CD79, CD56, and CD117.[3] Cutaneous EMP usually appears as subcutaneous nodules measuring 1-5 cm in the thoracic and abdominal regions, but it can also occur on the face, neck, and extremities. The life expectancy after diagnosis is less than 12 months. Immunohistochemistry helps differentiate a neoplastic process from a reactive one, typically showing positivity for CD38, CD79, and CD138, negativity for CD19 and CD20, and unusually high positivity for CD56.[4]

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A 67-year-old woman presented with lower back pain and was found to have anemia. Further tests revealed Immunoglobulin A (IgA)/kappa MM. The patient's diagnostic and follow-up values are shown in Table 1. Positron emission tomography and computed tomography (PET-CT) showed multiple lytic bone lesions and increased FDG uptake in the bone marrow. The patient was classified as Durie-Salmon stage 3 and received four cycles of bortezomib-cyclophosphamide-dexamethasone chemotherapy. Due to disease progression after chemotherapy, treatment was continued with carfilzomib-lenalidomide-dexamethasone. Autologous stem cell transplantation was performed following an excellent partial response. Two months post-transplant, the patient developed nodular lesions in the frontoparietal area, abdomen, and the middle finger of the right hand (Figure 1, Figure 2, Figure 3). A biopsy confirmed plasmablast infiltration, demonstrating kappa monoclonality and IgG heavy chain expression, consistent with cutaneous involvement of MM. Although the patient achieved a complete biochemical response, PET-CT showed no evidence of disease outside the skin lesions.

The patient was started on daratumumab-lenalidomide-dexamethasone treatment. As the existing skin lesions did not improve and were painful, radiation therapy was begun. In the 8th month of treatment, new lesions appeared, leading to the discontinuation of lenalidomide and a switch to daratumumab-pomalidomide-dexamethasone. However, during the 1st month of this new treatment, the patient experienced severe coronavirus disease-2019 (COVID-19) pneumonia, which resulted in stopping the medications. During follow-up, widespread large masses of plasma cells were observed on the skin, despite no biochemical evidence of disease. Because the patient could not access CAR-T cell therapy due to fi-

TABLE 1: Bone marrow biopsy and lab results

Parameter	Initial diagnosis	After ASCT treatment	After extramedullary relapse
IgA	8.01 g/L	1.93 g/L	0.17 g/L
Free kappa/lambda	134	1.4	9.3
Serum immunofixation electrophoresis	KLC band	Weak IgG lambda band	No monoclonal band
Urine immunofixation	KLC band	No monoclonal band	No monoclonal band
Creatinine	0.87 mg/dL	0.64 mg/dL	0.97 mg/dL
Corrected calcium	9.7 mg/dL	8.7 mg/dL	9.1 mg/dL
Hemoglobin	10.9 g/dL	11.8 g/dL	11.3 g/dL
Beta-2 microglobulin	7.98 mg/L	2.69 mg/L	Not evaluated
Cytogenetics-del(17p)	Negative	Not assessed	Negative
Cytogenetics-t(4;14)	Negative	Not assessed	Negative
Cytogenetics-t(11;14)	Negative	Not assessed	Negative
Bone marrow biopsy	70% plasma cells, kappa clonal	No residual plasma cell disease	15% plasma cells, kappa clonal

The numerical value of the M-peak in protein electrophoresis was not measured, so it remains unknown. IgA: Immunoglobulin A; IgG: Immunoglobulin G; KLC: Kappa light chain; Lambda: Lambda light chain; del(17p): Deletion of the short arm of chromosome 17; t(4;14): Translocation between chromosomes 4 and 14; t(11;14): Translocation between chromosomes 11-14

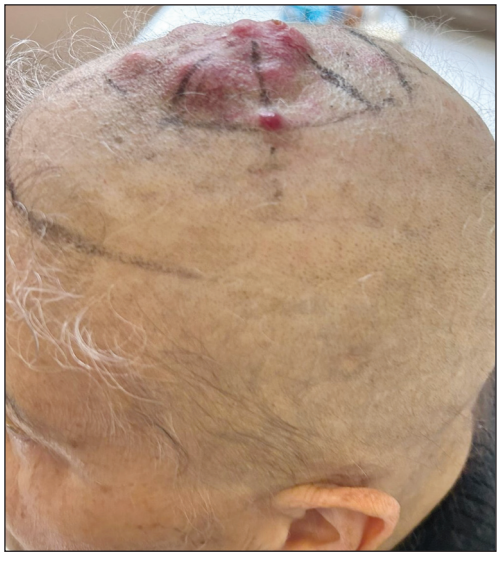

FIGURE 1: The lesion forming on the head of the case

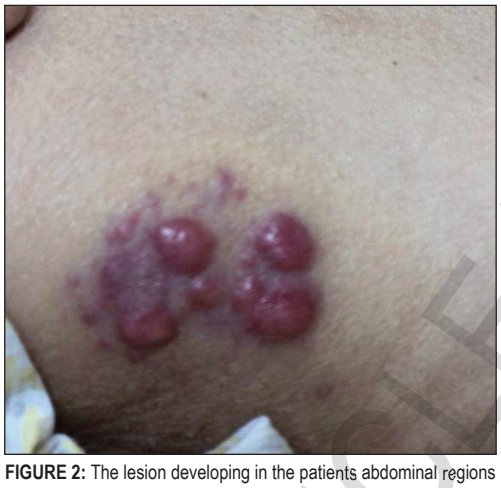

FIGURE 2: The lesion developing in the patients abdominal regions

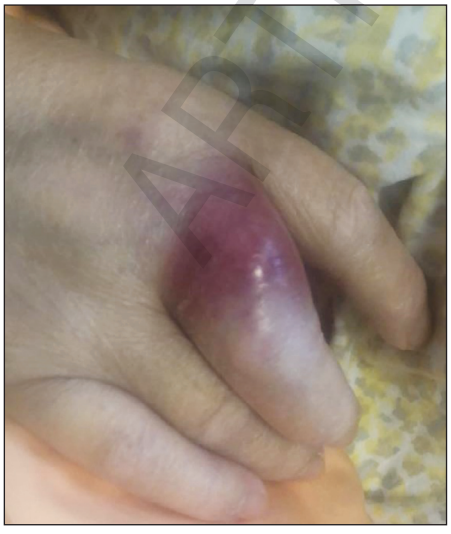

FIGURE 3: The lesion forming on the right finger of the case

nancial reasons, treatment was started with the carfilzomib-pomalidomide-dexamethasone-cisplatin-doxorubicin-etoposide-cyclophosphamide (KPD-PACE) protocol.[12] After the 1st cycle, the lesions rapidly improved; however, new lesions appeared during the 2nd cycle. The daratumumab-bendamustine was included in the treatment plan, but the disease progressed, leading to the patient's death.

Ethics committee approval was received for this study from Dr. Sadi Konuk Training and Research Hospital with protocol code 2023/331 (date: August 21. 2023). Written informed consent was obtained from the patient for publishing this case report and the accompanying images.

DISCUSSION

This case report describes a rare skin manifestation called EMP, which developed as a secondary condition in a patient with relapsed MM after autologous stem cell transplantation. The lesions appeared as purplish nodules with petechial features, located in the frontoparietal region, the middle finger of the right hand, the umbilical area, and the left leg. Primary extramedullary plasmacytoma (EMD) in MM is associated with an aggressive disease course, drug resistance, and poor prognosis, with short survival despite the use of new therapeutic agents.[13,14] EMD most commonly occurs in the liver or lymph nodes, while skin involvement is rare; only about 2-4% of EMPs involve the skin.[15] Skin involvement in MM is uncommon, usually appears in advanced stages, and is typically linked to a poor prognosis, with an average survival of approximately 1 year after diagnosis.[4] Patients with EMD tend to have very short overall survival and often present with high-risk cytogenetic abnormalities such as t (4;14), t (14;16), gain (1q21), or del (17p).[14]

Some studies suggest that EMD may be more responsive to novel agents than standard chemotherapy.[15] However, there is currently no data on the efficacy of daratumumab, a new anti-CD38 monoclonal antibody, in treating cutaneous EMD. Our patient had previously received bortezomib, lenalidomide, and carfilzomib, and due to the relapse interval after these treatments, a daratumumab-based therapy was initiated.

Previous studies have reported that these lesions are most often located in the chest and abdominal wall and usually appear as papulonodular lesions. In our case, immunohistochemical analysis showed IgG and CD38 positivity, while CD20, CD30, CD45, CD56, and Epstein-Barr Virus were negative. Similarly, Yoo et al. reported CD38 positivity and CD56 negativity in their case.[6] Additionally, in the same study, the patient developed EMP 8 months after autologous transplantation, whereas in our case, EMP was observed at 2 months post-transplantation.[6] Two months after autologous transplantation, nodular lesions appeared in the frontoparietal region of the head, anterior abdominal wall, and middle finger of the right hand (Figure 1, Figure 2, Figure 3). Skin biopsy showed plasmablastic infiltration, KLC restriction, and IgG heavy chain expression; these findings confirmed cutaneous involvement of MM. PET-CT imaging revealed no systemic disease other than the skin lesions. Accordingly, the patient was treated with daratumumab and lenalidomide. Although no new lesions appeared, the existing ones remained, leading to radiotherapy. The lack of new lesions over an 8-month follow-up indicates a limited but clinically meaningful response to daratumumab.

Notably, this case showed a switch from IgA to IgG, likely indicating clonal evolution and the development of therapy-resistant subclones linked to poor prognosis.[9] Additionally, moderate CD38 expression may have contributed to the less-than-ideal response to daratumumab.[10] The treatment was also complicated by severe COVID-19 pneumonia, which probably sped up disease progression due to therapy interruption.[11]

CONCLUSION

The patient's limited financial resources restricted access to CAR-T cell therapy, limiting treatment options for managing aggressive cutaneous relapse. Despite intensive salvage regimens such as KPD-PACE and daratumumab-bendamustine, disease progression could not be stopped. This case highlights the challenges of treating rare forms of MM with skin involvement and emphasizes the poor prognosis linked to such presentations.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Yağmur Berktaş;* ***Design:*** *Sümeyye Hanoğlu, Yağmur Berktaş, Emine Gültürk;* ***Control/Supervision:*** *Yağmur Berktaş, Sümeyye Hanoğlu;* ***Data Collection and/or Processing:*** *Yağmur Berktaş, Sümeyye Hanoğlu, Emine Gültürk;* ***Analysis and/or Interpretation:*** *Sümeyye Hanoğlu, Yağmur Berktaş;* ***Literature Review:*** *Yağmur Berktaş, Sümeyye Hanoğlu;* ***Writing the Article:*** *Yağmur Berktaş, Sümeyye Hanoğlu;* ***Critical Review:*** *Sümeyye Hanoğlu, Emine Gültürk, Yağmur Berktaş;* ***References and Fundings:*** *Sümeyye Hanoğlu, Yağmur Berktaş, Emine Gültürk;* ***Materials:*** *Yağmur Berktaş, Sümeyye Hanoğlu, Emine Gültürk.*

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