

CASE REPORT

Open Access



# Extramedullary relapse of Immunoglobulin A-kappa myeloma manifesting as plasmacytoma of the pleura without bone marrow involvement and following autologous bone marrow transplant: a case report

Alireza Rezvani<sup>1,2</sup>, Reza Shahriarirad<sup>2,3</sup>, Mohammad Javad Fallahi<sup>4</sup> and Ali Zeighami<sup>2,3\*</sup>

## Abstract

**Background** Recurrence of multiple myeloma is among the most challenging issues for patients and treating physicians reported after autologous stem cell transplantation. However, extramedullary involvement after chemotherapy and transplantation has been rarely reported, especially as pleural manifestations. Protein electrophoresis indicated immunoglobulin A monoclonal kappa plasma cell neoplasm in our case.

**Case presentation** A 48-year-old middle-eastern man was referred to our clinic with cough, dyspnea, fever, and left side pleural effusion. A year after chemotherapy and autologous bone marrow transplantation, the patient presented with features in favor of pleural relapse, without bone marrow involvement. Protein electrophoresis demonstrated immunoglobulin A monoclonal kappa plasma cell neoplasm in our case. The patient was effectively treated with dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, and etoposide with no notable adverse effects.

**Conclusion** Physicians should be aware of various presentations of multiple myeloma relapse, especially in autologous stem cell transplantation patients. Atypical and unique presentations such as the pleural involvement warrant further reporting of evidence to provide early management and treatment options.

**Keywords** Multiple myeloma, Bone marrow transplantation, Pleural effusion, Recurrence, Case report

## Background

Extramedullary plasmacytoma is defined as monoclonal plasma cell foci outside the bone marrow that do not affect the bone marrow or have other systemic symptoms of multiple myeloma [1, 2]. With advancements in the medicine and treatment options for cancer patients, the management and treatment for recurrence of multiple myeloma (MM) are still among the most challenging issues for the patients and the treating physician. Malignant plasma cells in MM generally develop within the bone marrow, yet they can proliferate in extramedullary sites [3].

\*Correspondence:

Ali Zeighami  
alizeighami2009@gmail.com

<sup>1</sup> Bone Marrow Transplantation Center, Nemazi Hospital, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>2</sup> Thoracic and Vascular Surgery Research Center, Shiraz University of Medical Science, Shiraz 71936-13311, Iran

<sup>3</sup> Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran

<sup>4</sup> Department of Internal Medicine, Nemazee Hospital, Shiraz University of Medical Sciences, Shiraz, Iran



© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

Conservative treatment for MM is still ineffective, although high-dose therapy with autologous stem cell support may be beneficial [4]. Relapses occur in 63% of autologous stem cell transplant recipients, with 4% of them being related to pulmonary diseases [5, 6]. We reported a unique instance of multiple myeloma presenting with pleural recurrence without bone marrow involvement.

### Case presentation

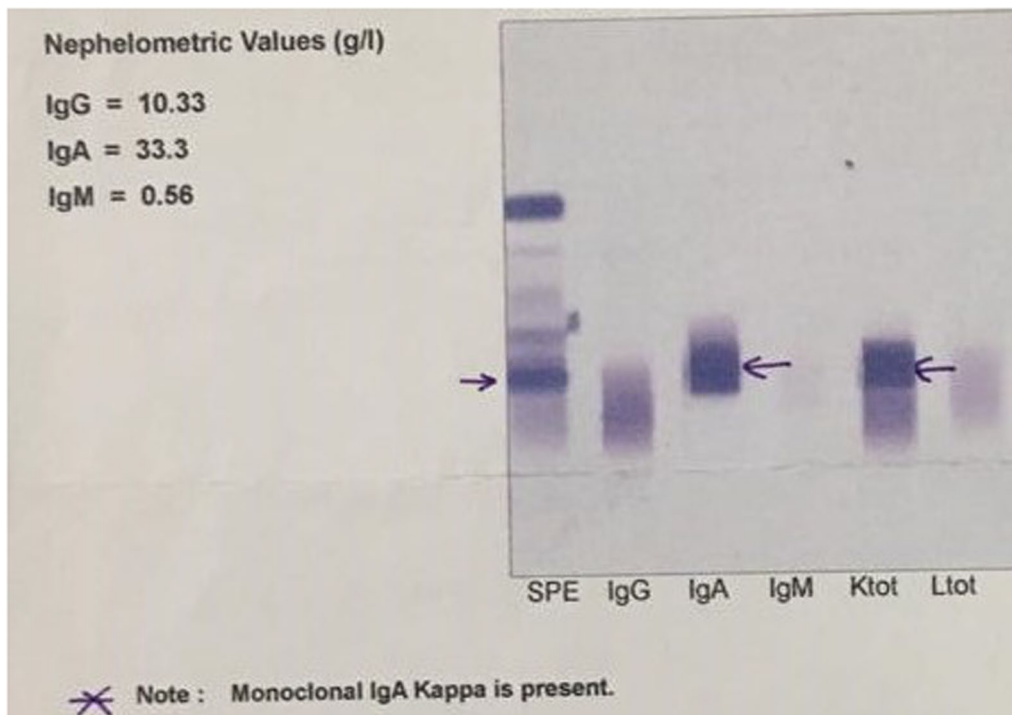
A 48-year-old Persian man was referred to our clinic with cough and dyspnea. He was relatively well until 1 year ago, with no significant past medical history, when he developed generalized bone pain, especially in the back and chest wall area. After numerous workups, a diagnosis of immunoglobulin A (IgA) monoclonal kappa plasma cell neoplasm (Fig. 1) was made, and treatment was started. Initially, the patient was treated with multiple cycles of bortezomib, dexamethasone, and lenalidomide (VRD). The patient was able to withstand all four cycles of the VRD regimen. Complete remission was obtained without any major adverse effects after the first course of therapy. After autologous stem cell transplantation, lenalidomide maintenance treatment was administered.

The patient was considered in remission until 2 months before his admission to our center, when he developed cough, dyspnea, fever, and left side pleural effusion. He

underwent reevaluation with suspicion of disease relapse, in which pleural plasmacytoma was detected without bone marrow involvement. No evidence of remarkable monoclonal band was observed in the protein electrophoresis (albumin: 65.7%; gamma: 13.4%; alpha 1: 3.2%; alpha 2: 8%; beta 1: 5.5%; beta 2: 4.2%; total protein: 6.6). (Table 1) Chest sonography showed left side moderate-to-severe pleural effusion. The insertion of a pleural drainage needle catheter on the patient revealed crimson pleural fluid. Multiple polypoid nodules and masses were seen in the parietal pleura and diaphragm (Fig. 2) during pleuroscopy. A pleural biopsy of affected pleural nodules revealed plasma cell infiltration.

Fluorodeoxyglucose–positron emission tomography (FDG–PET) scan findings showed hypermetabolic multi-organ involvement in the left parietal and visceral pleura, pericardial invasion, left diaphragmatic crus lymph node involvement in thoracic (bilateral internal mammary, prevascular) and also abdominal (celiac) regions, as well as bone involvement (in T5, L4, and right pubis) and in left side oblique muscles (Fig. 3).

The diagnosis of relapse was based on pleuroscopy and biopsy, and immunoelectrophoresis; therefore, in terms of the aggressiveness of the tumor, the patient received salvage therapy DT-PACE (a regimen consisting of six chemotherapy drugs: dexamethasone, thalidomide, cisplatin, adriamycin, cyclophosphamide, and etoposide)

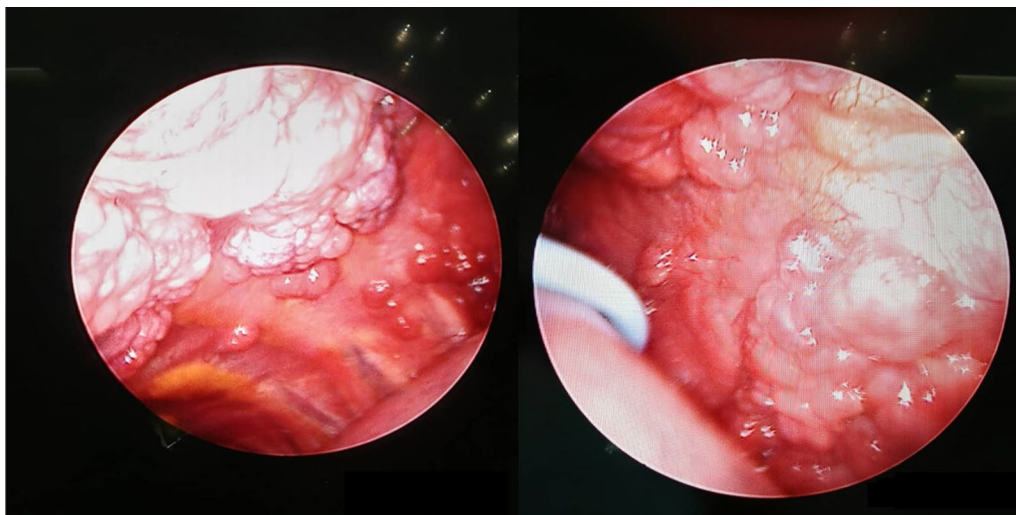


**Fig. 1** Protein electrophoresis demonstrating Immunoglobulin A (IgA) monoclonal kappa plasma cell neoplasm, arrows demonstrate the accumulation of IgA kappa

**Table 1** Laboratory and paraclinical features of a male case of extramedullary relapse of Immunoglobulin A-kappa myeloma manifesting as isolated plasmacytoma of the pleura

Test	Value	Adult reference range
Immunofixation electrophoresis		
IgG	10.33	6.58–18.37
IgA	33.33	0.71–3.60
IgM	0.56	0.40–2.63
Serum protein electrophoresis		
Albumin; g/dl (%)	4.34 (65.7%)	4.02–4.76 (55.8–66.1%)
Alpha 1; g/dl (%)	0.21 (3.2%)	0.21–0.35 (2.9–4.9%)
Alpha 2; g/dl (%)	0.53 (8.0%)	0.51–0.85 (7.1–11.8%)
Beta 1; g/dl (%)	0.36 (5.5%)	0.34–0.52 (4.7–7.2%)
Beta 2; g/dl (%)	0.28 (4.2%)	0.23–0.47 (3.2–6.5%)
Gamma; g/dl	0.88 (13.4%)	0.80–1.35 (11.1–18.8%)
A/G ratio	1.92	
Total protein; g/dl	6.6	6.6–8.3
Urine biochemistry		
Urine microalbumin (random); mg/L	23	<20
Urine creatinine (random); mg/L	151	25–400
Microalbumin/creatinine ratio	0.15	
Urine analysis		
Albumin	1+	–
Blood	1+	–
Protein	1+	–
Other		
ESR; mm/hour	18	0–15
Immunohistochemistry bone marrow		
CD138	Positive in sheet of plasma cells	
CD19	Positive in benign lymphoid nodule	
CD20	Positive in benign lymphoid nodule	
Kappa	Positive	
Lambda	Negative	

A/G: albumin to globulin; ESR: Erythrocyte sedimentation rate; IgA: Immunoglobulin A; IgG: Immunoglobulin G; IgM: Immunoglobulin M



**Fig. 2** Pleuroscopy demonstrating plasmacytoma of the pleura



**Fig. 3** Fluorodeoxyglucose–positron emission tomography (FDG–PET) scan of a 48 year old male patient diagnosed with extramedullary relapse of IgA-kappa myeloma manifesting as isolated plasmacytoma of the pleura, demonstrating hypermetabolic multiorgan involvement in the left parietal and visceral pleura, pericardial invasion, left diaphragmatic crus lymph node involvement in thoracic (bilateral internal mammary, prevascular) and also abdominal (celiac) regions, as well as bone involvement (in T5, L4, and right pubis) and in left side oblique muscles

due to unavailability of second-line standard treatment in our center. The patient had no serious adverse effects, the medication was effective, and he became asymptomatic. After 6 months, the patient had no concerns or issues during his follow-up appointments. The patient had immunoelectrophoresis, free light chain, and beta-2 microglobulin testing as part of his follow-up examination and is now a candidate for a second autologous transplant. Figure 4 demonstrates the timeline of events in our patient.

### Discussion and conclusion

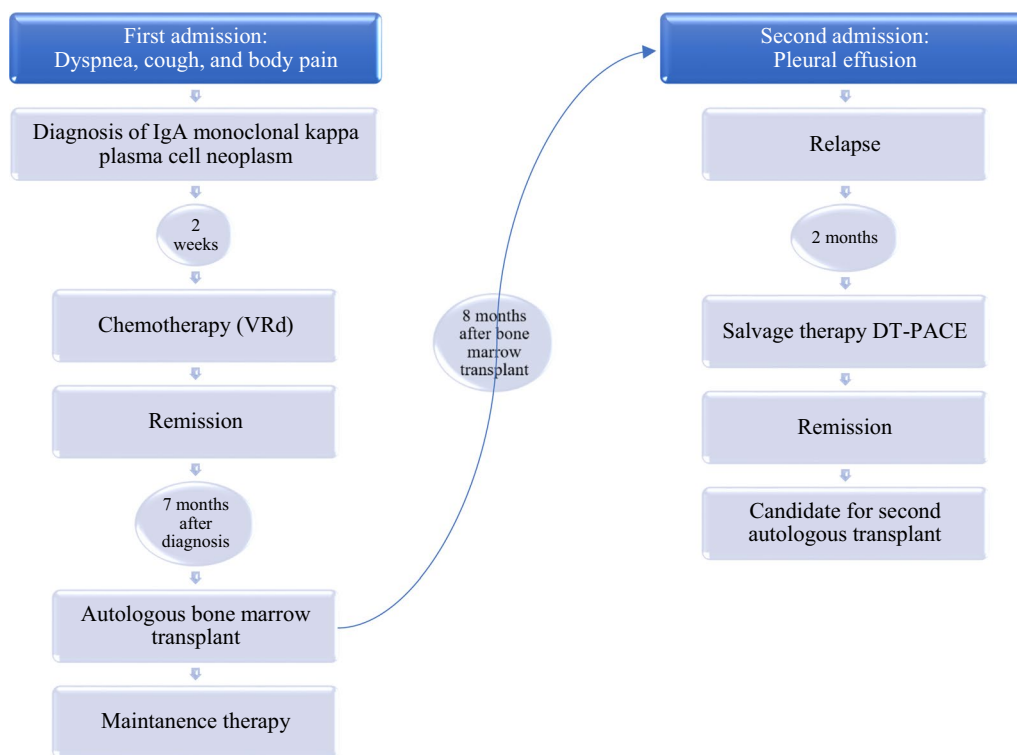
In patients with MM, autologous stem cell transplantation (ASCT) after high-dose chemotherapy increases the rate of complete response and survival compared with conventional chemotherapy. Therefore, this approach is more frequently used as the first line of therapy for eligible symptomatic MM patients under the age of 70 years, and has become the standard treatment for this group

of patients. However, relapse of the disease is one of the main problems commonly reported.

Pleural plasmacytomas are extremely rare and account for around 3–6% of extramedullary disease in MM patients. Based on a recent literature review, less than ten cases of pleural plasmacytomas due to MM have so far been reported [7]. Our case reported an extramedullary relapse, particularly in the pleura, after ASCT. Other studies have reported a higher incidence of extramedullary relapse after ASCT. We believe there are several features which make our case valuable to the present literature, including the location, molecular findings, and most importantly subsequent to treatment. Our case was an extramedullary relapse in a patient who had undergone both chemotherapy and ASCT, with an initial presentation of the pleura, and respiratory symptoms of cough and dyspnea, and an immunoglobulin report demonstrating an IgA-kappa plasmacytoma. We believe that each of these three features are important and have been scarcely reported in literature. In a study by Cerny *et al.*, over a 9-year period (1999–2007), only six (3.9%) out of 156 MM patients developed extramedullary relapse [8]. None of the relapses were reported in the pleura or lungs, and only two were IgA-kappa, of which one was in the liver and the other in the stomach and colon.

A report by the Spanish registry regarding 560 MM patients showed 52% relapse or progression of the disease at a median follow-up of 23 months after transplantation, with a median overall survival of 52 months and an estimated progression-free survival of 33 months [9]. One of the hypotheses for the reason for relapse is that genetic abnormalities in plasma cells induce their infiltration into areas less affected by the immune system and used for medical purposes, such as the pleura, therefore multiplying and triggering extracellular relapse. Plasmacytoma relapse without evidence of systemic myeloma progression, occurring either as an isolated phenomenon or concurrent with systemic relapse, has been reported in ASCT and allogeneic bone marrow transplantation (BMT), ranging from 7% to 35% [10–12]. The most frequent (66%) pattern of relapse is the classical pattern, presenting as a progressive increase of monoclonal component and medullary plasmacytic infiltration.

Pleural involvement is rarely mentioned in the medical literature, especially after treatment. Zeiser *et al.* reported extramedullary recurrence in the lungs, soft tissue, bone, and pericardium after ASCT, and also in the lungs, soft tissue, skin, central nervous system, and pericardium following allogeneic BMT [5]. Feng *et al.* [13] reported solitary pleural plasmacytomas, which presented with massive pleural effusion without evidence of monoclonal gammopathy after local radiotherapy and systemic chemotherapy. Saidane *et al.* reported a



**Fig. 4** Clinical timeline of patient diagnosed with extramedullary relapse of IgA-kappa myeloma manifesting as isolated plasmacytoma of the pleura. DT-PACE dexamethasone, thalidomide, cisplatin, adriamycin, cyclophosphamide, and etoposide, IgA immunoglobulin A, VRD velcade (bortezomib) + revlimid (lenalidomide) + dexamethasone

case of pleural involvement after treatment of cutaneous MM [14]. Also, Harith Al-Ataby *et al.* [15] reported a case of pleural plasmacytomas due to MM relapse that was asymptomatic. However, their case was 9 months after chemotherapy and radiotherapy, while in our case, the relapse was detected 8 months after ASCT and VRD therapy.

In the Spanish registry study, extramedullary recurrence was identified in around 7% of patients who received ASCT (14% of relapsed patients), with numerous or single lesions presenting with null or minimal paraprotein. [9] Terpos *et al.* also reported that 9.5% of patients who underwent ASCT and 6% of those who received an allograft BMT relapsed as an extramedullary plasmacytoma. [10] Allogeneic BMT is linked with an immunologic graft-versus-myeloma effect, therefore, it is expected to be accompanied by lower rates of disease recurrence. [16–18]

Protein electrophoresis demonstrated IgA monoclonal kappa plasma cell neoplasm in our case. Previous reports of extramedullary relapse of IgA-lambda myeloma were reported as intracranial plasmacytomas or pancreatic involvement [19, 20]. A report by Boyle on the impact of severe isotype paired suppression, as measured by IgA Hevylite, on survival, showed that severe

hypogammaglobulinemia indicates a dismal prognosis in patients with IgA MM, and that IgA isotype paired suppression is prognostic at the time of presentation among patients with IgA MM [21]. Furthermore, Alyea *et al.* reported no significant correlation between IgA isotype with progression-free survival and overall survival [4].

The treatment of extramedullary plasmacytomas in the setting of MM relapse is rather challenging. Regarding the aggressiveness of the tumor, the patient received salvage therapy DT-PACE (a regime consisting of six chemotherapy drugs: dexamethasone, thalidomide, cisplatin, adriamycin, cyclophosphamide, and etoposide), due to unavailability of second-line standard treatment such as carfilzomib in our center. The patient developed no significant side effects, and the treatment was successful. The DT-PACE treatment is an effective combination chemotherapy for high-risk patients like ours. In 2003, Lee *et al.* indicated that this regimen may induce a 32% partial response and a 16% full and near-complete response in high-risk and advancing patients with cancer [22]. Carfilzomib is a second-generation proteasome inhibitor. The phase 3 ENDEAVOR study included a combination of carfilzomib and dexamethasone (KD) [23]. The carfilzomib-lenalidomide-dexamethasone (KRD) and lenalidomide-dexamethasone

therapies were evaluated in the ASPIRE study [24]. The results of both studies supported using carfilzomib as a means of extending life. Our treatment followed guidelines reported by the National Comprehensive Cancer Network (NCCN) and Oxford Myeloma group [25, 26]. As mentioned in the NCCN, we initially treated our patients with VRD therapy. During the recurrence, despite the fact that current guidelines recommended triplet regimens (NCCN) for refractory patients, we chose the DT-PACE combination for our patient due to the lack of second-line treatment options in our center, and also the aggressiveness of the tumor based on the patients dyspnea as well as the course of the disease [25, 26]. Carfilzomib is a highly successful treatment for extramedullary plasmacytomas such as MM. A KD chemotherapy treatment was found to be beneficial for a patient with pleural and cardiac involvement by Espaol *et al.* in 2017 [27]. In a separate case report, the authors noted that the combination of carfilzomib and lenalidomide was effective in plasmacytomas when administered without radiation to a patient with brain involvement [28]. Three months of DT-PACE therapy resulted in a complete response in our patient. Despite introducing several new treatments, MM management is still a challenging issue.

In conclusion, this case is remarkable since our patient received both chemotherapy and ASCT due to IgA-kappa MM, but still relapsed with extramedullary manifestations, particularly pleural involvement, which is a rare type and was remarkably observed in the FDG-PET scan. The prevalence of extramedullary MM relapses has grown in recent years, and clinicians should be familiar with the many manifestations of this illness, particularly in ASCT patients, to give early management and treatment options.

#### Abbreviations

ASCT	Autologous stem cell transplantation
BMT	Bone marrow transplantation
DT-PACE	Dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, etoposide
FDP-PET	Fluorodeoxyglucose-positron emission tomography
IgA	Immunoglobulin A
MM	Multiple myeloma

#### Acknowledgements

None to declare.

#### Author contributions

AR and MJF made the disease diagnosis and carried out the patient's treatment course. RS and AZ collected the data. MJF performed the bronchoscopy. RS and AZ drafted the manuscript. All authors proofread and accepted the final version of the manuscript.

#### Funding

No financial support was received for this case report.

#### Availability of data and materials

All data regarding this case has been reported in the manuscript. Please contact the corresponding author if you are interested in any further information.

#### Declarations

##### Ethics approval and consent to participate

Written informed consent was obtained from the patient in our study. The purpose of this research was completely explained to the patient, and they were assured that their information would be kept confidential by the researcher. The present study was approved by the Medical Ethics Committee of the academy.

##### Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

##### Competing interests

The authors declare that they have no competing interests.

Received: 7 January 2022 Accepted: 6 January 2023

Published online: 10 February 2023

#### References

- Alexiou C, Kau RJ, Dietzfelbinger H, Kremer M, Spiess JC, Schratzenstaller B, Arnold W. Extramedullary plasmacytoma: tumor occurrence and therapeutic concepts. *Cancer*. 1999;85(11):2305–14.
- Luh S-P, Lai Y-S, Tsai C-H, Tsao TC-Y. Extramedullary plasmacytoma (EMP): report of a case manifested as a mediastinal mass and multiple pulmonary nodules and review of literature. *World J Surg Oncol*. 2007;5(1):123.
- Sunnecioglu A, Ekin S, Bayram I, Ekinci O, Bugday IB. Endobronchial plasmacytoma in patient with multiple myeloma. *Clin Respir J*. 2017;11(6):1057–9.
- Alyea E, Weller E, Schlossman R, Canning C, Mauch P, Ng A, Fisher D, Gribben J, Freeman A, Parikh B, *et al.* Outcome after autologous and allogeneic stem cell transplantation for patients with multiple myeloma: impact of graft-versus-myeloma effect. *Bone Marrow Transpl*. 2003;32(12):1145–51.
- Zeiser R, Deschler B, Bertz H, Finke J, Engelhardt M. Extramedullary vs medullary relapse after autologous or allogeneic hematopoietic stem cell transplantation (HSCT) in multiple myeloma (MM) and its correlation to clinical outcome. *Bone Marrow Transpl*. 2004;34(12):1057–65.
- Ebrahimi A, Ahmadi H, Pourfraidon Ghasrodashti Z, Tanide N, Shahriarad R, Erfani A, Ranjbar K, Ashkani-Esfahani S. Therapeutic effects of stem cells in different body systems, a novel method that is yet to gain trust: a comprehensive review. *Bosn J Basic Med Sci*. 2021;21(6):672–701.
- Yeoh K-W, Thitsar SM, Master Z, Loh Y, Chen Y, Nagarajan C, Tin K-M, Catter D, Mikhael G. Pleural plasmacytomas-the role of radiotherapy. *Br J Haematol*. 2020;190(3):e160–2.
- Cerny J, Fadare O, Hutchinson L, Wang SA. Clinicopathological features of extramedullary recurrence/relapse of multiple myeloma. *Eur J Haematol*. 2008;81(1):65–9.
- Alegre A, Granda A, Martinez-Chamorro C, Diaz-Mediavilla J, Martinez R, Garcia-Larana J, Lahuerta JJ, Sureda A, Blade J, de la Rubia J, *et al.* Different patterns of relapse after autologous peripheral blood stem cell transplantation in multiple myeloma: clinical results of 280 cases from the Spanish Registry. *Haematologica*. 2002;87(6):609–14.
- Terpos E, Rezvani K, Basu S, Milne AE, Rose PE, Scott GL, Rahemtulla A, Samson D, Apperley JF. Plasmacytoma relapses in the absence of systemic progression post-high-dose therapy for multiple myeloma. *Eur J Haematol*. 2005;75(5):376–83.
- Moreau P, Bataille R, Mahé B, Milpied N, Harousseau J. High-dose melphalan is not associated with extramedullary relapses in high-risk multiple myeloma. *J Clin Oncol*. 1993;11(9):1832–1832.

12. Lokhorst HM, Meuwissen OJ, Verdonck LF, Dekker AW. High-risk multiple myeloma treated with high-dose melphalan. *J Clin Oncol*. 1992;10(1):47–51.
13. Feng PH, Huang CC, Wang CW, Wu YK, Tsai YH. Solitary pleural plasmacytomas manifested as a massive pleural effusion without evidence of monoclonal gammopathy. *Respirology*. 2008;13(5):751–3.
14. Saidane O, Slouma M, Haouet S, Abdelmoula L. Cutaneous and pleural involvement in a patient with multiple myeloma. *BMJ Case Rep*. 2015;2015:bcr2015211197.
15. Al-Ataby H, Al-Tkrit A, Ali S, Seneviratne C, Omballi M. Pleural plasmacytomas in a patient with multiple myeloma relapse. *Respir Med Case Reports* 2022;2022:101777.
16. Or R, Mehta J, Naparstek E, Okon E, Cividalli G, Slavin S. Successful T cell-depleted allogeneic bone marrow transplantation in a child with recurrent multiple extramedullary plasmacytomas. *Bone Marrow Transpl*. 1992;10(4):381–2.
17. Verdonck LF, Lokhorst HM, Dekker AW, Nieuwenhuis HK, Petersen EJ. Graft-versus-myeloma effect in two cases. *Lancet*. 1996;347(9004):800–1.
18. Tricot G, Vesole DH, Jagannath S, Hilton J, Munshi N, Barlogie B. Graft-versus-myeloma effect: proof of principle. *Blood*. 1996;87(3):1196–8.
19. Annibali O, Marchesi F, Petrucci MT, Tirindelli MC, Avvisati G. Relapse of IgA  $\lambda$  multiple myeloma presenting as obstructive jaundice and abdominal pain. *Oncol Res Treatment*. 2009;32(3):119–21.
20. Waterhouse DF, Moloney GA, Gargoum FS, Hayden PS, O’Gorman T. Extramedullary relapse of IgA-lambda myeloma after recent bortezomib therapy: a case report. *Cases J*. 2009;2(1):7456.
21. Boyle EM, Fouquet G, Guidez S, Bonnet S, Demarquette H, Dulery R, Herbaux C, Noel MP, Manier S, Schraen S, et al. IgA kappa/IgA lambda heavy/light chain assessment in the management of patients with IgA myeloma. *Cancer*. 2014;120(24):3952–7.
22. Lee CK, Barlogie B, Munshi N, Zangari M, Fassas A, Jacobson J, van Rhee F, Cottler-Fox M, Muwalla F, Tricot G. DTPACE: an effective, novel combination chemotherapy with thalidomide for previously treated patients with myeloma. *J Clin Oncol*. 2003;21(14):2732–9.
23. Dimopoulos MA, Moreau P, Palumbo A, Joshua D, Pour L, Hajek R, Facon T, Ludwig H, Oriol A, Goldschmidt H, et al. Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR): a randomised, phase 3, open-label, multicentre study. *Lancet Oncol*. 2016;17(1):27–38.
24. Stewart AK, Rajkumar SV, Dimopoulos MA, Masszi T, Spicka I, Oriol A, Hajek R, Rosinol L, Siegel DS, Mihaylov GG, et al. Carfilzomib, lenalidomide, and dexamethasone for relapsed multiple myeloma. *N Engl J Med*. 2015;372(2):142–52.
25. Oxford Myeloma Group Network site specific group (NSSG)—Haematology-VDTPACE/ DTPACE [<https://nssg.oxford-haematology.org.uk>]
26. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Multiple Myeloma Version 2 [[www.nccn.org/patients](http://www.nccn.org/patients)]
27. Espanol I, Romera M, Gutierrez-Meca MD, Garcia MDC, Tejedor A, Martinez A, Ibanez J, De Arriba F, Minguela A, Iturbe T, et al. Carfilzomib and dexamethasone for extramedullary myeloma with pleuropericardial involvement. *Clin Case Reports*. 2017;5(8):1258–60.
28. Mele G, Pastore D. Efficacy of carfilzomib, lenalidomide, and dexamethasone for extramedullary intracranial localization of multiple myeloma. *Case Reports Hematol*. 2018;2018:2312430.

## Publisher’s Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more [biomedcentral.com/submissions](https://biomedcentral.com/submissions)

