Case Report

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# Central nervous system relapse in multiple myeloma: An unusual complication

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**Abstract:**

Central nervous system involvement in multiple myeloma (MM) is rare and carries a very poor prognosis. We report the case of a 62-year-old man diagnosed with MM who received induction chemotherapy with bortezomib, cyclophosphamide, and dexamethasone and achieved very good partial response. He developed seizures and altered sensorium while on maintenance chemotherapy. Magnetic resonance imaging of the brain showed leptomeningeal enhancement, and cerebrospinal fluid cytology was positive for plasma cells. His general condition worsened, and he died before starting any specific treatment.

**Keywords:**

Central nervous system, cerebrospinal fluid positivity, multiple myeloma

## Introduction

Multiple myeloma (MM) is a malignancy characterized by the proliferation of clonal plasma cells in the bone marrow with monoclonal protein in the serum and/or urine along with organ dysfunction. Extramedullary disease in MM is uncommon and is seen in 3%–5% and involves the skin, nasopharynx, larynx, upper respiratory tract, and central nervous system (CNS).[1]

CNS involvement is rather uncommon and is described in about 1% of the MM, and in one study, the prevalence was 7%.[2,3]

The CNS involvement can occur at the time of initial diagnosis or at the time of progression of MM and present with parenchymatous lesions and/or leptomeningeal involvement diagnosed by imaging tests, cerebrospinal fluid (CSF) study, or biopsy.[4] They present with neurological symptoms such as headache and visual disturbances and are often mistaken for medical complications seen in MM.

Leptomeningeal disease in MM is extremely rare and, in one series, constituted only 15% of the MM patients with CNS involvement and carried a bad prognosis with overall survival of 5.8 months.[3] The optimal treatment for CNS disease in MM has not been defined and usually includes systemic chemotherapy, intrathecal chemotherapy, radiotherapy, and autologous stem cell transplantation.[4]

We report the case of a 62-year-old gentleman diagnosed with MM who relapsed with CNS involvement while on maintenance chemotherapy.

## Case Report

A 62-year-old man presented with back pain and decreased urine output of 2-week duration. Clinical examination showed pallor, bilateral pedal edema, and tenderness of dorsolumbar spine. Hemogram showed that hemoglobin was 9.9 g/dl, total leukocyte

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count was 12,000/mm,[3] platelet count was 270000/mm$^3$, and erythrocyte sedimentation rate was 120 mm/h. The serum creatinine was 5.9 mg/dl, serum calcium was 12.7 mg/dl, serum albumin was 2.8 mg/dl, serum lactate dehydrogenase (LDH) was 453 u/l, and serum beta-2 microglobulin was 18 mg/L. Serum electrophoresis showed a monoclonal band measuring 7.6 g/dl. The serum immunoglobulin (Ig) G was 4500 mg/dl, IgA was 76 mg/dl, and IgM was 50 mg/dl; kappa-to-lambda light chain ratio was 150. Immunoelectrofixation showed a monoclonal band corresponding to IgG kappa [Figure 1]. A skeletal survey showed multiple punched-out lytic lesions involving the skull, multiple vertebrae, and pelvic bones. Bone marrow aspiration showed 90% plasma cells, and immunohistochemical studies showed kappa light chain restriction [Figure 2]. A final diagnosis of MM – IgG kappa, Stage III Revised International Staging System with all the CRAB features (Hypercalcemia, renal dysfunction, anemia, and lytic bone lesions) was made. He was started on induction chemotherapy with bortezomib, cyclophosphamide, and dexamethasone. Evaluation after six cycles showed very good partial response with an M protein of 0.31 gm/dl, 4% plasma cell on bone marrow aspiration. He refused autologous stem cell transplantation and further chemotherapy due to personal reasons. He was started on maintenance with bortezomib. Two months later, he reported with altered sensorium, irrelevant talk, seizures, and features of bronchopneumonia. Ophthalmic fundus showed bilateral papilledema. Magnetic resonance imaging of the brain showed bilateral extensive sulcal exudates with leptomeningeal enhancement. CSF study showed elevated glucose (200 mg/dl) and protein (148 mg/dl). CSF cytology showed atypical plasmacytoid cells with immature nuclei suggestive of plasma cell myeloma infiltration [Figure 3]. Further investigations did not reveal disease elsewhere. The bone marrow was normal. In view of the relapse involving the CNS, he was planned for salvage chemotherapy and cranial irradiation. He was started on broad-spectrum intravenous antibiotics for bronchopneumonia. However, his condition worsened, and he died 8 months after the initial diagnosis.

## Discussion

MM typically presents with skeletal symptoms such as pain due to fractures and lytic bone lesions, infections related to immunoparesis, renal failure, and neurologic symptoms due to uremia or hypercalcemia, spinal cord compression, cranial nerve infiltration, or peripheral neuropathy**.** CNS involvement is extremely rare in MM. It can be due to direct extension of skull lesion to the brain, due to plasmacytoma arising in dura or mucosa of the nasopharynx and parenchymal lesions without an extension from the abovementioned areas or by hematogenous dissemination.

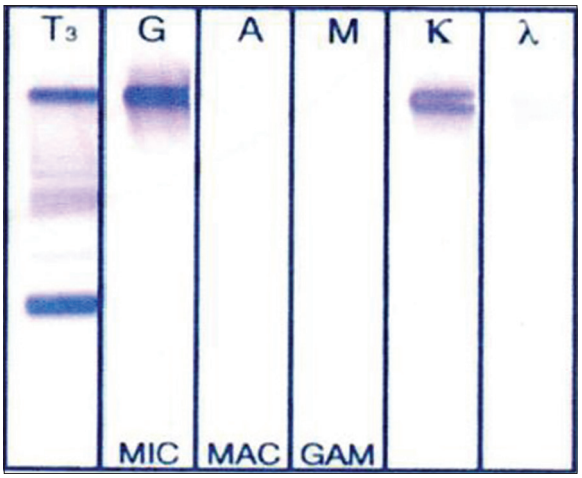


**Figure 1:** Serum immunoelectrofixation showing monoclonal band corresponding to immunoglobulin G kappa

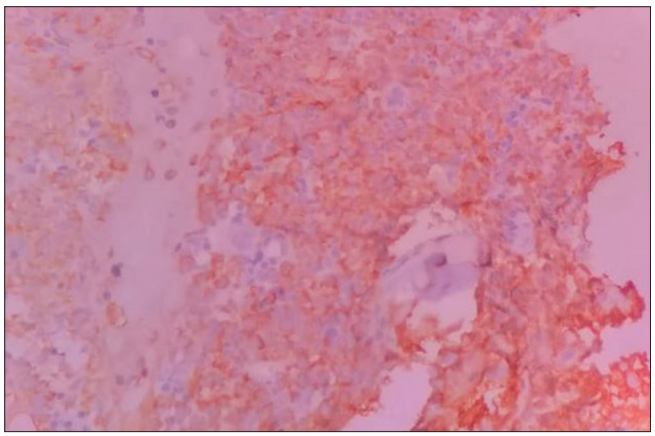

**Figure 2:** Immunohistochemistry of the bone marrow showing kappa light chain restriction (Immunohistochemistry × 1000)

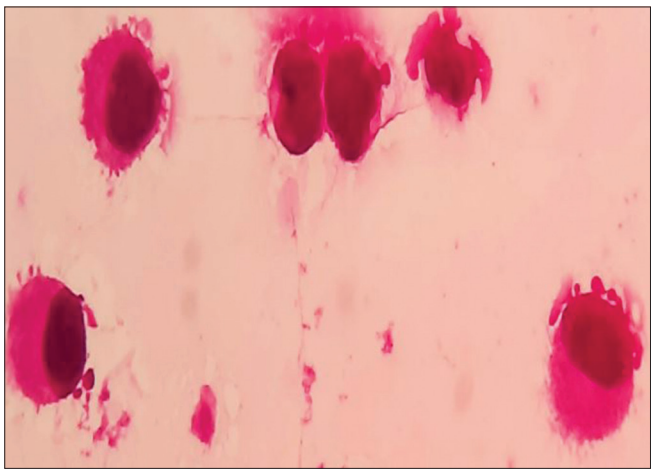

**Figure 3:** Cerebrospinal fluid cytology smear showing atypical plasma cells (pap staining × 100)

CNS Involvement by MM can result in headache, confusion, somnolence, seizures, or cranial nerve palsies. Magnetic resonance imaging is a sensitive imaging modality to detect CNS involvement. Diagnosis is

confirmed by the presence of plasma cells in the CSF. Stereotactic tissue biopsy may be needed if results are inconclusive**.** A retrospective analysis on CNS involvement in MM included 172 patients.[5] The exact etiology of CNS spread is not clear. Deletions of chromosome 17p13.1 (p53) have been found in 89% of the CNS MM patients.[6] Other possible risk factors include extramedullary disease, plasmablastic morphology, cytogenetic abnormalities, high tumor load, increased LDH levels. Our patient had a high initial tumor load and elevated LDH, which might have predisposed to CNS spread. Predictors of adverse outcomes in these patients included at least one previous line of anti-MM therapy and more than one cytogenetic abnormality in MM cells.[5]

CNS involvement confers a very poor prognosis with a median survival of 2 months.[3] There is no consensus on the management of these patients. Systemic treatment, alone or combined with intrathecal chemotherapy and radiotherapy, is the preferred modality of treatment. However, the drugs that are approved for the treatment of relapsed MM, such as the proteasome inhibitors (bortezomib, carfilzomib, and ixazomib), do not cross the blood–brain barrier. Immunomodulatory agents such as lenalidomide and pomalidomide which can penetrate the blood–brain barrier have been used as systemic agents.[7] Pomalidomide has resulted in the disappearance of myeloma cells from CSF and is more effective than other agents in patients harboring 17p deletion.[8] There are case reports of successful treatment of CNS MM with second-generation proteasome inhibitor marizomib and anti-CD 38 antibody daratumumab.[9,10] High-dose chemotherapy with agents crossing blood–brain barrier along with intrathecal chemotherapy followed by cranial irradiation and/or autologous bone marrow transplantation for responders has also been tried.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

## References

1. Nieuwenhuizen L, Biesma DH. Central nervous system myelomatosis: Review of the literature. Eur J Haematol 2008;80:1-9.
2. Varettoni M, Corso A, Pica G, Mangiacavalli S, Pascutto C, Lazzarino M. Incidence, presenting features and outcome of extramedullary disease in multiple myeloma: A longitudinal study on 1003 consecutive patients. Ann Oncol 2010;21:325-30.
3. Dias AL, Higashi F, Peres AL, Cury P, Crusoé EQ, Hungria VT. Multiple myeloma and central nervous system involvement: Experience of a Brazilian center. Hematol Transfus Cell Ther 2018;40:30-6.
4. Chen CI, Masih-Khan E, Jiang H, Rabea A, Cserti-Gazdewich C, Jimenez-Zepeda VH, *et al*. Central nervous system involvement with multiple myeloma: Long term survival can be achieved with radiation, intrathecal chemotherapy, and immunomodulatory agents. Br J Haematol 2013;162:483-8.
5. Jurczyszyn A, Grzasko N, Gozzetti A, Czepiel J, Cerase A, Hungria V, *et al*. Central nervous system involvement by multiple myeloma: A multi-institutional retrospective study of 172 patients in daily clinical practice. Am J Hematol 2016;91:575-80.
6. Chang H, Sloan S, Li D, Keith Stewart A. Multiple myeloma involving central nervous system: High frequency of chromosome 17p13.1 (p53) deletions. Br J Haematol 2004;127:280-4.
7. Mussetti A, Dalto S, Montefusco V. Effective treatment of pomalidomide in central nervous system myelomatosis. Leuk Lymphoma 2013;54:864-6.
8. Leleu X, Karlin L, Macro M, Hulin C, Garderet L, Roussel M, *et al*. Pomalidomide plus low-dose dexamethasone in multiple myeloma with deletion 17p and/or translocation (4;14): IFM 2010-02 trial results. Blood 2015;125:1411-7.
9. Badros A, Singh Z, Dhakal B, Kwok Y, MacLaren A, Richardson P, *et al*. Marizomib for central nervous system-multiple myeloma. Br J Haematol 2017;177:221-5.
10. Elhassadi E, Murphy M, Hacking D, Farrell M. Durable treatment response of relapsing CNS plasmacytoma using intrathecal chemotherapy, radiotherapy, and Daratumumab. Clin Case Rep 2018;6:723-8.