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Rare case of CNS myeloma, successfully treated with intrathecal chemotherapy, selinexor and craniospinal radiotherapy

Linas Davainis[1], Agata Bruzgul[2]

[1] Hematology, Oncology and Transfusion Medicine Center, Vilnius university Hospital Santaros Klnikos, Vilnius, Lithuania
[2] Vilnius university, Faculty of Medicine, Vilnius, Lithuania

Introduction

Extramedullary CNS multiple myeloma is rare (<1%) and associated with poor survival, with a reported median overall survival of approximately 7 months (1). Current evidence supports a multimodal treatment strategy combining CNS-active systemic therapy, intrathecal chemotherapy, and radiotherapy (2-4). Emerging data suggest that newer agents such as selinexor may be particularly relevant due to CNS penetration (5). Here, we present a rare case of CNS multiple myeloma successfully treated with a multimodal approach incorporating selinexor, supporting its potential role in achieving durable disease control.

Case presentation

We present a 78-year-old male with relapsed/refractory IgG kappa multiple myeloma, stage III, and a six-year disease history. Cytogenetic analysis revealed t(11;14) and complex karyotype with 13 chromosome monosmy, del16q, dup9q. Over the disease course, he received multiple lines of therapy, including VTD, KRD, and daratumumab-based regimens, achieving only transient responses before developing refractory disease. AutoHSCT was not performed in any step of therapy due to advanced age and frailty.

In late 2025, the patient developed progressive neurological symptoms, including profound sensorineural hearing loss, dizziness, visual field disturbances, and gait ataxia. Magnetic resonance imaging demonstrated a lesion in the medial aspect of the right orbit, along with multifocal extra-axial and leptomeningeal involvement, including lesions along cranial nerves VII–VIII, consistent with disseminated CNS myeloma (image 1). Cerebrospinal fluid (CSF) analysis confirmed CNS involvement, with elevated protein levels (up to 1.04 g/L), increased intrathecal IgG, and marked pleocytosis with a predominance of clonal plasma cells (up to 84%) (image 2), consistent with leptomeningeal disease. At the time of CNS progression, systemic disease remained controlled, with no detectable M-protein despite rising involved free light chain levels.

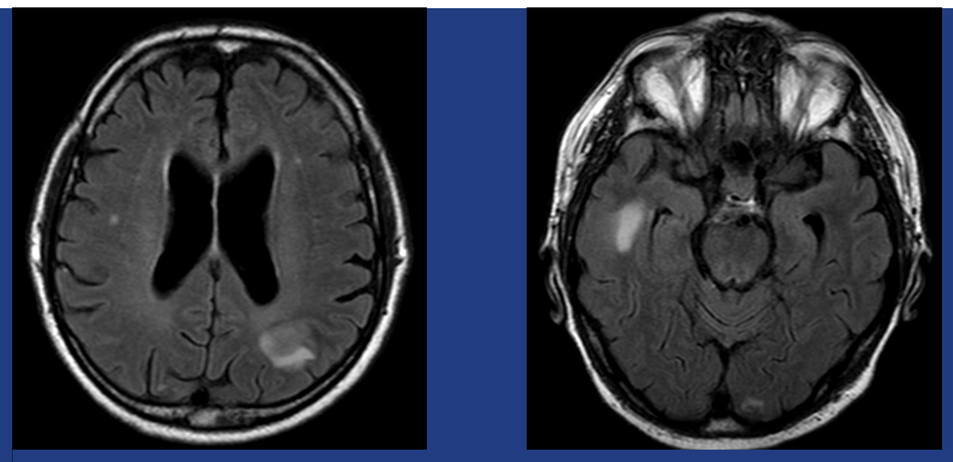


Image 1. Brain MRI showing parenchymal lesions in the left temporal and right occipital lobes.

A CNS-directed multimodal salvage strategy was initiated, consisting of daratumumab, selinexor, and dexamethasone (Dara–SelDex), combined with intrathecal triple chemotherapy (methotrexate 12 mg, cytarabine 30 mg, and dexamethasone 4 mg) and craniospinal irradiation (figure 1). Repeated flow cytometry demonstrated loss of CD38 expression on clonal plasma cells, likely reflecting prolonged prior anti-CD38 exposure, so daratumumab was discontinued.

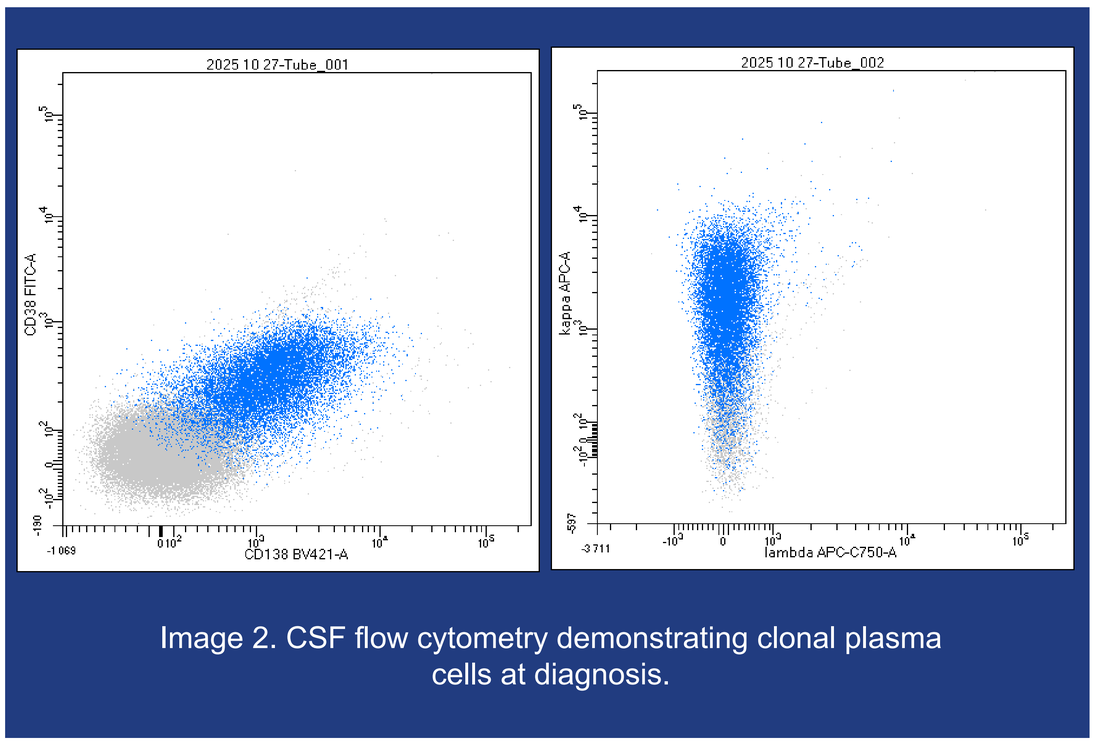


Image 2. CSF flow cytometry demonstrating clonal plasma cells at diagnosis.

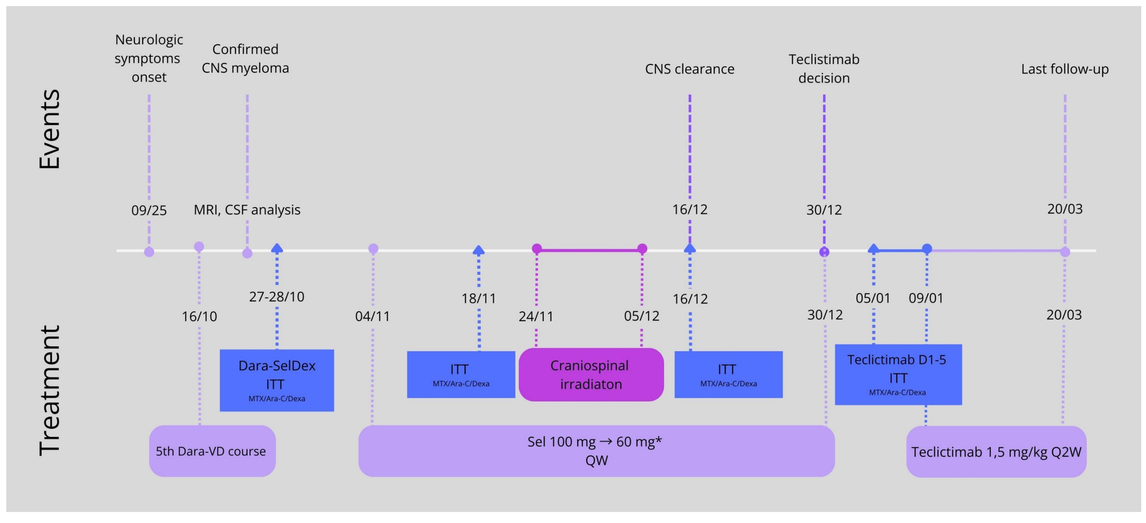
Selinexor dose gradually decreased from initial 100mg QW to 60mg QW, because of side effects (hyperemesis, hyponatremia, anorexia). Selinexor discontinued rapidly after CNS remission achieved.

This multimodal approach resulted in complete CNS disease clearance, confirmed by two consecutive negative CSF evaluations, including flow cytometry with no detectable clonal plasma cells. Previously mentioned neurological symptoms partially improved.

Following CNS disease control, BCMA-directed therapy with teclistamab was initiated as consolidation. Treatment was administered. No cytokine release syndrome (CRS) or immune effector cell-associated neurotoxicity syndrome (ICANS) was observed.

At last follow-up, CNS disease remained in remission, with maintained systemic disease control under ongoing teclistamab therapy.

Figure 1. Patient timeline and treatment course.



Abbreviations: Ara-C - cytarabine; CNS - central nervous system; CSF - cerebrospinal fluid; Dara-SelDex - daratumumab, selinexor, dexamethasone; Dara-VD - daratumumab, bortezomib, dexamethasone; ITT - intrathecal chemotherapy; MRI - magnetic resonance imaging; MTX - methotrexate.

Conclusions

CNS involvement in multiple myeloma represents a rare and aggressive manifestation with no established standard of care. This case highlights that CNS progression may occur despite controlled systemic disease, underscoring the role of the central nervous system as a sanctuary site. A multimodal approach combining intrathecal chemotherapy, radiotherapy, and CNS-penetrant systemic therapy can achieve complete CNS disease eradication even in heavily pretreated patients. Selinexor may represent a particularly valuable option in this setting, enabling effective CNS control and facilitating transition to BCMA-directed immunotherapy or any other maintenance therapy, which can maintain systemic disease response.

Contact

L. Davainis, MD, linas.davainis@santa.lt

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