COMy

The 6th World Congress on

CONTROVERSIES IN MULTIPLE MYELOMA (COMy)

CENTRAL NERVOUS SYSTEM MYELOMA TREATED WITH VENETOCLAX: A CASE REPORT

Virág Réka Szita[1], Alexandra Balogh[1], Ágota Szepesi[2], Péter Farkas[1], Tamás Masszi[1], Gergely Varga[1]

[1]3rd Department of Internal Medicine, Semmelweis University
[2]1st Department of Pathology and Experimental Cancer Research

Introduction

Central nervous system (CNS) involvement in multiple myeloma is a rare form of extramedullary manifestation, occurring in less than 1% of cases. Treatment is a challenge due to a host of reasons: no randomized, controlled data are available; CNS involvement most often occurs in the relapsed/refractory setting; proteasome inhibitors – except marizomib – do not cross the blood-brain barrier; and common intrathecally used drugs have little anti-myeloma potency. Despite some promising results recently achieved mainly with anti-CD38 antibodies, most authors report a disheartening median overall survival of only 2-3 months in cases with leptomeningeal spread.[1] Venetoclax is an emerging agent for the treatment of 11;14 translocated myeloma, but although there is anecdotal information about its usefulness in leptomeningeal chronic lymphoid leukemia[2], there has been to date no data about its use in CNS myeloma.

Case report

Diagnosis Our 70-year-old patient was diagnosed with multiple myeloma following a pathological humerus fracture in January 2019. Prognostic evaluation showed ISS stage 3 disease and (11;14) translocation. Therapy was initiated with VTD, then switched to VRD because of neuropathy. After reaching VGPR however, kappa light chain levels started reincreasing. Considering the cytogenetical makeup of the patient, he received venetoclax and having reached VGPR again, we proceeded to ASCT in July 2019, after which PET-CT control described complete regression of the lytic lesions.

First relapse In October 2019 the patient presented with rapidly deteriorating neurological symptoms, convulsions and unconsciousness. Liquor sampling was carried out, testing negative with PCR for meningeal pathogens. Flow cytometry performed from the sample found 91% plasma cells in spite of close to normal FLC levels. Combined treatment was initiated with daratumumab, venetoclax and dexamethasone and the patient responded promptly, recovering without any neurological sequelae. MRI (Fig. 1.) described edema in the right frontal lobe (arrows), as well as periventricular FLAIR inhomogenities (arrowheads) consistent with leptomeningeal myeloma infiltration. Morphological resolution of the lesions was confirmed by control MR imaging two months later (Fig. 2.).

Second relapse After five uneventful months of venetoclax- daratumumab therapy, the patient experienced severe headache, nausea and vertigo in March, 2020. Emergent MRI found no lesions compared to the previous imaging (Fig. 3.), but liquor evaluation and flow cytometry showed 40% CSF plasmocytes. Due to financial constraints, daily venetoclax dose had been lowered to 300 mg od. with the concomitant use of clarithromycin (250 mg od.), a common antibiotic known to increase serum venetoclax levels fourfold. Careful history taking at the time of this second relapse revealed that the patient had stopped taking clarithromycin some time before. Daratumumab was then stopped due to the apparent refractoriness; reinstitution of clarithromycin with 400 mg venetoclax dose once again (together with full dose lenalidomide and 8 mg weekly dexamethasone) resulted in prompt resolution of the patient's neurological symptoms.

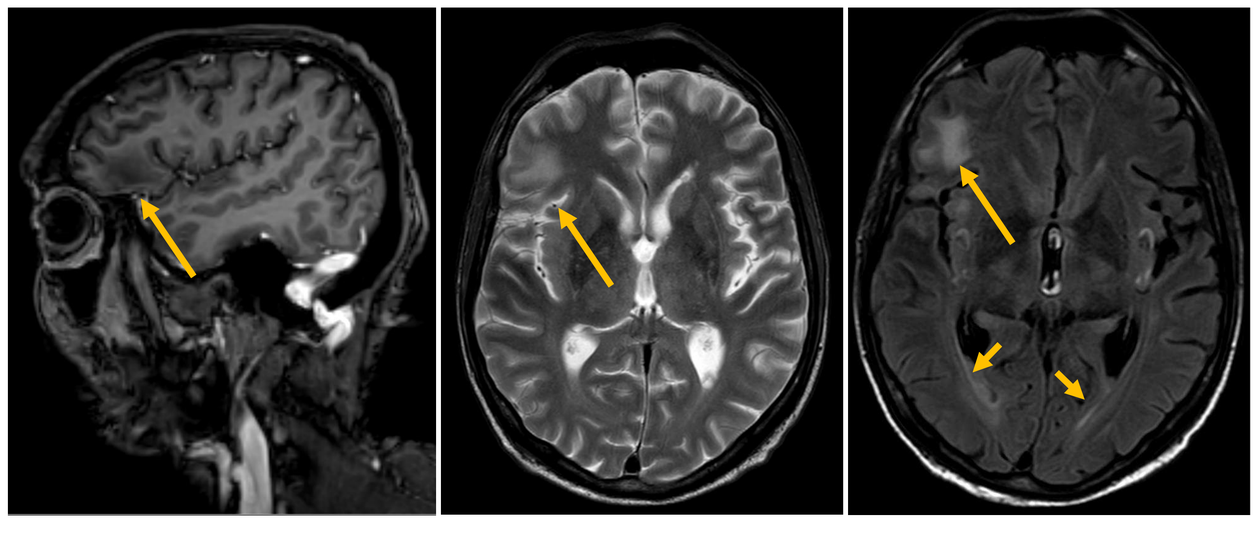

Fig. 1. Edema in the right frontal lobe and FLAIR inhomgenities on MRI (T1, T2 weighted and FLAIR images)

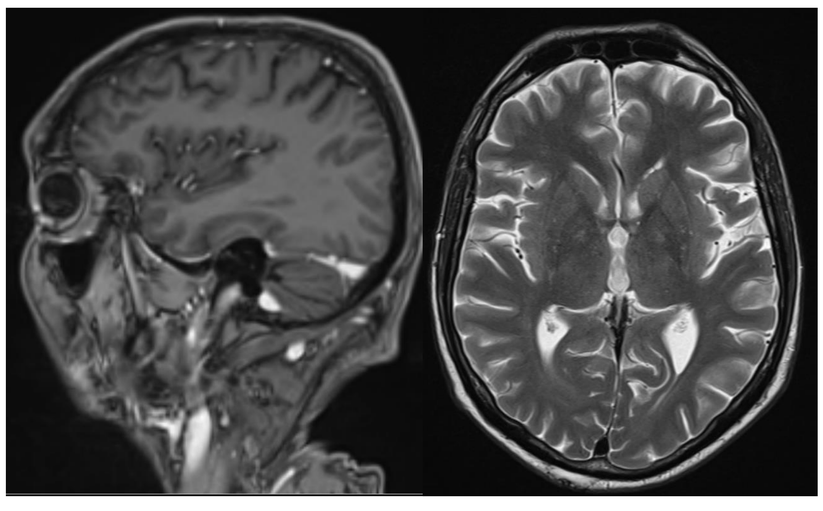

Fig. 2. Complete resolution of all morphological findings on control MRI (T1 and T2 weighted images)

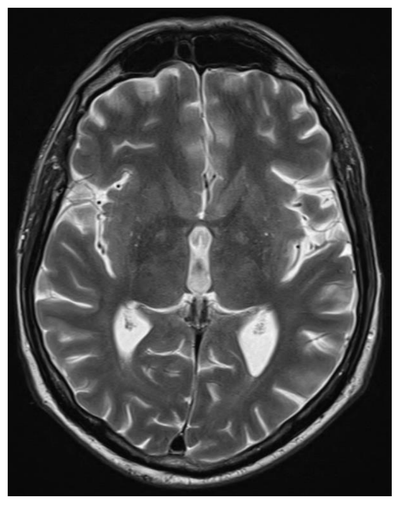

Fig. 3. No lesions were found at second relapse (T2 weighted images)

Conclusion

Our patient keeps enjoying very good quality of life more than six months after his initial central nervous system relapse, taking only oral maintenance. Our case shows that although venetoclax is probably not a cure on its own for t(11;14) myeloma, it may be surprisingly effective, even in cases with highly unfavorable prognosis. The venetoclax dose utilized in myeloma studies is higher than that standardly used in CLL and AML, which can be an obstacle when negotiating reimbursement with health authorities. As our case so unexpectedly demonstrated, this higher plasma level is absolutely necessary for clinical effectivity. In our case, treatment of this particular patient was only possible by utilizing an otherwise not recommended combination with clarithromycin, retrospectively justified with the good outcome.

References

[1]Varga G, Mikala G, Gopcsa L, Csukly Z, Kollai S, Balázs G, Botond T, Wohner N, Horváth L, Szombath G, Farkas P, Masszi T. (2018) Multiple Myeloma of the Central Nervous System: 13 Cases and Review of the Literature. J Oncol. 2018 Apr 23;2018:3970169. doi: 10.1155/2018/3970169.

[2]Beziat, G., Gauthier, M., Protin, C., Oberic, L., Lerebours, F., Carlier, J., & Ysebaert, L. (2020). Venetoclax with high-dose methotrexate and rituximab seem effective and well-tolerated in the treatment of central nervous system involvement of chronic lymphocytic leukemia: A case report. Clinical Case Reports. doi: 10.1002/ccr3.2580