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IMAGES IN MEDICINE

Multiple Myeloma With Isolated Central Nervous System Relapse

Natasa-Eleni Loutsidi, Natali El Gotmi, Konstantinos Kaouranis, Themistoklis Karmiris, Sosana Delimpasi

Haematology-Lymphomas Department and Bone Marrow Transplant Unit, General Hospital of Athens "Evangelismos", Greece

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INTRODUCTION

Extramedullary disease is observed in up to 5% of Multiple Myeloma (MM) patients, resulting via hematogenous dissemination or through the bone cortex into the adjacent tissues. Central Nervous System involvement (CNS) in patients with MM is very rare, estimated at about 1% and it portends a very poor prognosis, due to frequent treatment failure with an Overall Survival (OS) of around 2 months. The infiltration can be diagnosed at the time of diagnosis of MM or during its progression. Nevertheless, it occurs frequently in refractory disease or during relapse. CNS-MM has an earlier age of onset (50-60 vs 65-70 years old) in contrast with the typical MM.[1,2] The diagnosis of CNS involvement is difficult and at the same time challenging, as it manifests itself with neurological symptoms, which can be interpreted as typical manifestations of myeloma or side effects of treatment. Symptoms may include visual changes, headache, confusion, impairment to speech, dizziness and radiculopathy. Somnolence and seizures may also occur in patients with intraparenchymal lesions. We present a case of a Caucasian male patient, 60 years old, diagnosed with MM in 2017, who had a second isolated relapse in the CNS.

METHODS

A 60-year-old man, with no personal history, was diagnosed on 10/2017 with MM, stage I according to ISS. He was treated with the VCD regimen (Bortezomib, Cyclophosphamide, Dexamethasone) and achieved complete remission. One year later, he relapsed with plasmacytomas in the thoracic spine. He refused Autologous Hematopoietic Stem Cell Transplantation and received 17 KRD cycles (Carfizomib, Lenalidomide, Dexamethasone). The patient achieved complete remission of plasmacytomas, underwent maintenance treatment with lenalidomide from 7/2020 and regular follow-up at the Outpatient Department. In October 2020 he presented with numbness in the left upper and lower extremity, gait instability and urinary cyst disorders. Computed Tomography (CT) scan of the brain was normal. Magnetic Resonacne Imaging (MRI) of lumbar spine was performed, which showed thickening in cauda equina roots. In the differential diagnosis, among others, there was leptomeningeal infiltration from MM. Laboratory testing was normal. It is worth mentioning, that serum immunofixation was negative for monoclonal paraprotein. Moreover, there was absence of bone marrow infiltration by plasma cells. Lumbar puncture was performed

Correspondence to:
Loutsidi Natasa-Eleni, MD,
Tel.: +30-6945123998,
E-mail: natloutsidi@gmail.com

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and the CSF study by flow cytometry did not detect plasma cells, however they were found after microscopy of CNS centrifuges. Figures 1, 2, 3 show infiltration of CNS with plasma cells in our patient. In general, imaging techniques, such as MRI of the brain and/or spine or CT scans are effective, but there

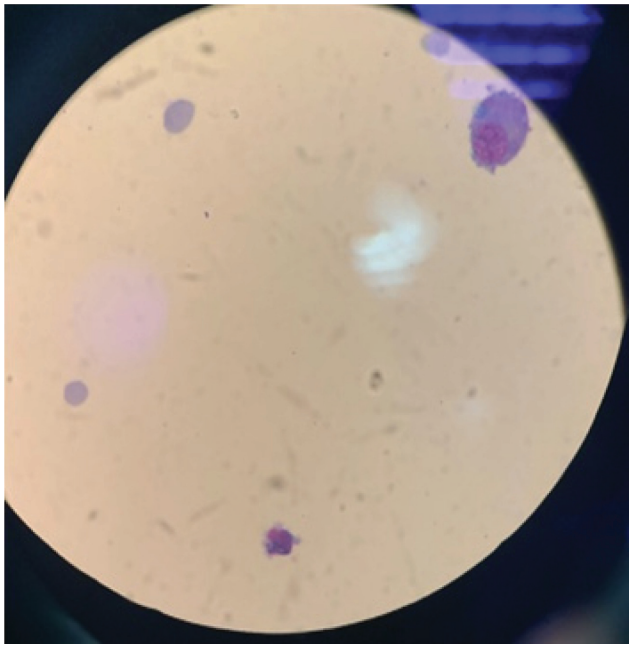

FIGURE 1.

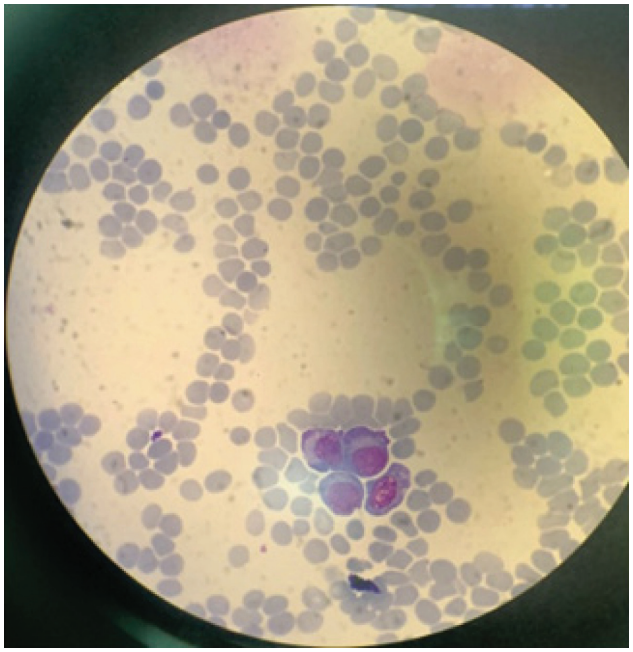

FIGURE 2.

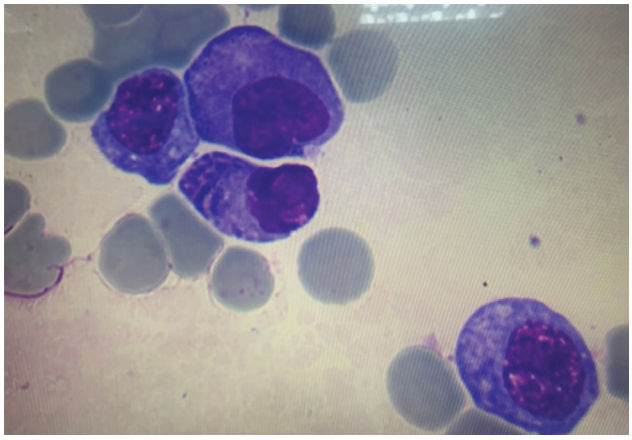

FIGURE 3.

is a false-negative result in about 10% of cases. Cerebrospinal fluid cytology and flow cytometry can detect atypical plasma cells and monoclonal CD38/CD138 expressing cells respectively, in approximately 90% of cases. It is worth mentioning that the loss of CD56 has been reported to be essential for extramedullary expansion of the neoplasm, especially for CNS involvement. Thus, CD56 is frequently positive in the neoplastic plasma cells intramedullary and negative in the neoplastic plasmablasts extramedullary, at time of relapse.[4] The diagnosis is confirmed by the presence of monoclonal immunoprotein and/or clonal plasma cells in CSF.[5] The normal lumbar CSF contains a cell count of up to 5/μL, consisting exclusively of lymphocytes and monocytes.[6] The patient was treated with a combination of intrathecal injections of chemotherapy (methotrexate 15 mg and dexamethasone 4 mg), 2 times per week until non-detection of plasma cells in CNS and systemic administration of Daratumumab (16 mg/Kg) every 15 days. He showed a dramatic improvement in symptoms, with a complete remission of neurological semiology.

DISCUSSION

CNS infiltration is rare and poorly described in the literature. The optimal treatment approach is not currently defined. The small number of patients diagnosed with this complication, does not allow to wage a high quality prospective clinical trial and so to have an evidenced-based approach to therapy.[5,7] The treatment must be aggressive due to frequent treatment failure and includes a combination of conventional chemotherapy, proteasome inhibitors, imids, autologous stem cell transplantation and radiotherapy. Moreover, intrathecal combinational chemotherapy (methotrexate 12.5 mg, aracytine 40 mg, dexamethasone 4 mg) is used in most of the cases. [7] The clinical manifestations are varied and heterogeneous,

resembling other common neurological diseases or side effects associated with chemotherapy, making differential diagnosis difficult. The gold-standard method for detecting CNS-MM is CSF cytology and flow cytometry. The sensitivity of MRI in solid tumors is much higher (85%) compared to hematologic malignancies (20-37%).[5]

CONCLUSION

Even in the age of new therapies, the prognosis of CNS-MM remains unfavorable, emphasizing the need to study the CNS penetration of existing drugs, but also the development of new ones with sufficient penetration into the CNS. Moreover, an innovative approach to treatment is obligatory. A better understanding of the biology of the disease could help identify high risk patients who may benefit from prophylaxis.

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