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Extended Abstract

Relapse of Mutiple Myeloma after Autologous Stem Cell Transplant Presenting with Central Nervous System Involvement without Evidence of Bone Marrow Involvement: The First Report of a Rare Clinical Entity

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Abstract

Multiple myeloma (MM) is characterized by uncontrolled clonal proliferation of plasma cells, mainly in bone marrow, and Extramedullary involvement is rare in MM. The incidence of extramedullary plasmacytomas is 7% to 18% at MM diagnosis and up to 20% at relapse.[1] The presence of extramedullary involvement in MM represents aggressive disease, and is associated with shorter overall and progression-free survival.[2] Extramedullary involvement commonly the nasopharyngeal, larynx, skin, upper respiratory tract, and central nervous system (CNS).[3]

The involvement of the CNS by MM, as defined by the presence of plasma cells in the cerebrospinal fluid (CSF) in a patient with MM, is considered extremely rare and is estimated only in 1% of patients. The best treatment regimen for MM with CNS involvement is still unknown and in most patients, the prognosis is unfavorable.[4] To date, there is no report of CNS involvement without evidence of systemic involvement in a known case with MM. To the best of our knowledge, this is the first published report of CNS involvement without evidence of systemic involvement in a known patient with MM relapse following autologous stem cell transplant.

Case Report

In October 2015, a 58-year-old male was presented to Hematology, Oncology and Stem Cell Transplantation Research Center; Tehran University of Medical Sciences, Tehran, Iran, with complaints of bone pain and decreased urine volume about 2 months prior to admission. Initial laboratory findings demonstrated a normocytic, normochromic anemia with a hemoglobin of 8.2 g/dL, a white blood cell count (WBC) of 6,500 cell/mm^3, and a platelets count of 245,000/mm. He had a creatinine of 4.2 mg/dL, calcium of 12.5 mg/dL, albumin of 3.7 g/dL, total protein of 11.7 g/dL, Beta-2 microglobulin of 13.8mg/L, and an erythrocyte sedimentation rate (ESR) of 135 mm/hr.

Serum protein electrophoresis (SPEP) and immunofixation electrophoresis (IFE) were performed that demonstrated immunoglobulin G kappa monoclonal gammopathy. A bone marrow biopsy showed more than 80 percent involvement by abnormal appearing plasma cells, confirmed by CD138+ immunohistochemical stain. In addition, a thorough cytogenetic evaluation revealed the deletion of 1q21 and t(4;14). A skeletal survey showed multiple well-defined lytic lesions (punched-out lesions) in the skull. Based on the Revised International Staging System (R-ISS), the diagnosis of stage III multiple myeloma was established.

The patient completed induction therapy with bortezomib-cyclophosphamide-dexamethasone (VCD) regimen and achieved a complete response after 4 courses of treatment. After the treatment period, the general condition of the patient was stabilized, the renal function was completely improved and all laboratory parameters were within the normal range. A repeat bone marrow biopsy following treatment did not show any evidence of multiple myeloma.In August 2016, the patient was scheduled for autologous bone marrow transplantation. Single-agent high-dose

Melphalan at the dosage of 200 mg/m^2 was used as a conditioning regimen prior to an autologous stem cell transplant. Bone marrow transplantation was performed successfully without any complication. Subsequently, the patient was placed on Lenalidomide maintenance (at a dose of 25 mg per day, on days 1 to 21 of each 28-day cycle) one month after the autologous bone marrow transplantation. On follow-up 5 months after the transplant, the patient had no clinical problems. After 5 months of transplantation, the patient suffered from severe headache and pelvic pain. In fundoscopic examinations, bilateral pupil edema was detected.

A lumbar puncture was performed and CSF smear revealed the presence of numerous plasma cells suggestive of CNS involvement (**Fig. 1**), which indicated a relapse of the MM. Interestingly, results of other diagnostic tests such as serum and urine protein electrophoresis with immunofixation, serum free light chains, and bone marrow aspiration and biopsy were all unremarkable.

The patient was consulted with Dr. James R. Berenson, who is the Founder, President and Chief Executive Officer of the Institute for Myeloma and Bone Cancer Research (IMBCR) and has specialized in the treatment of patients with multiple myeloma for more than 20 years in West Hollywood, California. Dr. Berenson suggested the DKBP-BD treatment regimen to be the best option in our patient.

The **DKBP-BD** regimen consisted of a 28-day cycle of **D**examethasone (40 mg as a 30-minute intravenous infusion on days 1, 8, 15, and 22), **K**yprolis® (Carfilzomib) [56 mg/m^2 as a 10-minute infusion on days 1, 8, and 15 (a dose of 20 mg per square meter was chosen as the starting dose)], **B**endeka® (bendamustine) [70 mg/m^2 as a 10-minute intravenous infusion on days 1 and 2], **P**omalyst® (pomalidomide) [4 mg once daily orally on days 1 to 21 of a 28-day cycle], **B**iaxin® (clarithromycin) [500 mg every 12 hours orally on days 1 to 28], **D**arzalex® (daratumumab) [16 mg/kg intravenous once weekly for 8 weeks (weeks 1 to 8); then 16 mg/kg every 2 weeks for 16 weeks (weeks 9 to 24); and then 16 mg/kg every 4 weeks thereafter]. Patient also received antiviral prophylaxis (acyclovir 200 mg orally twice daily), 81 mg of aspirin daily, Alpha-Lipoic Acid supplement 600 mg orally daily for the prevention of neuropathy (don't take it on the day of Kyprolis), Vitamin D and Calcium supplements, Allopurinol 300 mg orally daily, and zoledronic acid (Zometa) 4 mg intravenous once monthly.

Given the lack of some agents of this regime in Iran due to the unintended consequences of international sanctions, the patient was referred to Spain for receiving this treatment regimen.