[3] *Özel Emsey Hospital İç Hastalıkları, İstanbul, Türkiye*

Multiple sclerosis (MS) is a chronic, inflammatory, demyelinating disease of the central nervous system. Being an autoimmune disease, MS usually begins in young adulthood and may lead to permanent neurological damage over time. In the pathogenesis of the disease, immune responses mediated by T and B lymphocytes play a central role, causing damage to myelin and axonal structures[1]. Clinically, the most common form is relapsing-remitting MS (RRMS), while in some cases a transition to the secondary progressive MS (SPMS) form is observed over time[2]. The Expanded Disability Status Scale (EDSS) is widely used to assess neurological impairment in MS patients. This scale ranges from 0 to 10, with 0 indicating no neurological deficit. Higher scores represent greater neurological impairment. Disease-modifying therapies (DMTs), which modulate the immune system, are used in the treatment of MS. Major DMT agents include fingolimod, natalizumab, ofatumumab, ocrelizumab, siponimod, alemtuzumab, and interferon beta[3]. Despite high-efficacy treatments, a subset of patients continue to experience relapses and disease progression. Autologous hematopoietic stem cell transplantation (AHSCT) is a therapeutic option that aims to "reset" the immune system (immune reconstitution) by administering high-dose immunosuppressive therapy followed by reinfusion of the patient's own hematopoietic stem cells[4]. Recent prospective studies have demonstrated that AHSCT prevents relapses and ensures disease stabilization, especially in RRMS cases with high inflammatory activity and resistance to conventional therapies[5]. However, in progressive MS patients, while disease stabilization may occur, functional recovery remains limited. During the AHSCT process, hematopoietic stem cells are first mobilized into peripheral blood using cyclophosphamide and/or G-CSF, collected via apheresis, and cryopreserved with dimethyl sulfoxide (DMSO). Subsequently, high-dose chemotherapy (e.g., BEAM or CY+ATG regimen) is administered as a lymphoablative conditioning treatment, followed by reinfusion of the previously collected autologous stem cells[6]. In this study, we present two RRMS patients with refractory disease who underwent AHSCT in our clinic. Case-1: The first case is a 33-year-old female patient diagnosed with MS in 2018. She had been treated with DMT agents including ocrelizumab, without significant clinical response. With an EDSS score of 5, she was classified as RRMS, and AHSCT was planned. Mobilization was achieved with cyclophosphamide (2.4 g/m^2) and G-CSF. Hematopoietic stem cells were collected by apheresis and cryopreserved with DMSO. Following administration of the LEAM conditioning regimen (lomustine, etoposide, cytarabine, melphalan), a total of 4.54×10^6/kg autologous stem cells were reinfused on 05.06.2025. Neutrophil and platelet engraftment occurred on day 11 post-transplant. During the 3-month follow-up, no relapse occurred, and neurological status remained stable. **Case-2:** The second case is a 47-year-old male patient diagnosed with MS in 2014. He had received DMT agents including ocrelizumab and siponimod, without adequate response. With an EDSS score of 7 and progressive walking disability for the last 2 years, the patient was classified as SPMS, and AHSCT was planned. Mobilization was performed with cyclophosphamide (2.4 g/m^2) and G-CSF. Stem cells were collected via apheresis and cryopreserved with DMSO. After the LEAM conditioning regimen, a total of 5.19×10^6/kg autologous stem cells were reinfused on 19.01.2025. Neutrophil and platelet engraftment occurred on day 12 post-transplant. During the 8-month follow-up, no relapse occurred, and neurological status remained stable. **Discussion:** AHSCT has emerged as an effective treatment option for RRMS cases with high inflammatory activity refractory to conventional therapy. Studies have shown that AHSCT reconstitutes the immune system, thereby preventing relapses, avoiding new lesion development, and slowing neurological disability progression[7,8]. Clinical studies indicate that AHSCT can suppress MS disease activity in approximately 70–80% of patients for up to 5 years. This response rate is higher than with any other available MS treatment. While treatment-related mortality was reported as 3.6% in studies before 2005, this rate has decreased to approximately 0.3% in more recent studies[4]. A meta-analysis published in 2017 evaluated 764 MS patients who underwent AHSCT between 1995 and 2016, reporting event-free survival of 67%[9]. Another meta-analysis published in 2022, including 4,831 MS patients, found event-free survival in 68% of cases[10]. According to EBMT guidelines, cyclophosphamide (2–4.5 g/day) combined with G-CSF (5–10 μg/kg) is most commonly recommended for mobilization. Conditioning regimens typically include BEAM+ATG or cyclophosphamide+ATG[11]. In our cases, mobilization was performed with cyclophosphamide (2.2 g/day) followed by G-CSF (10 μg/kg). LEAM was used as the conditioning regimen, while ATG was not administered. It has been reported that AHSCT is more effective than DMTs in stabilizing neurological status, with ongoing trials continuing to evaluate this comparison[12]. Conclusion: AHSCT has shown favorable outcomes, particularly in RRMS patients. Large-scale analyses have demonstrated disease-free survival rates exceeding 60%. With advances in stem cell therapy, transplant-related mortality has significantly decreased. Therefore, AHSCT represents a safe and effective therapeutic option in RRMS.

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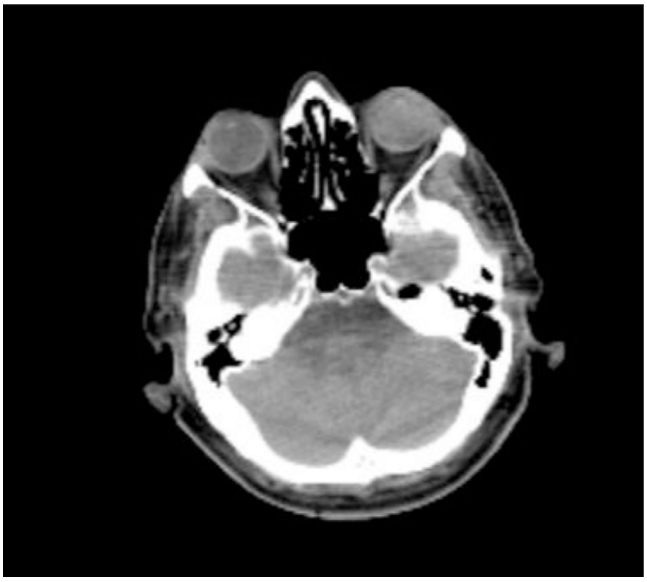
VITREORETINAL INVOLVEMENT IN NASAL CAVITY B-CELL LYMPHOMA: A RARE FORM OF RELAPSE

Songül Beskisiz Dönen *,
Vehbi Demircan Abdullah,
Karakuş Mehmet Orhan Ayyıldız

Dicle University Faculty of Medicine, Department of Hematology

Introduction: Non-Hodgkin lymphomas are malignant neoplasms of lymphoid tissue, and a subset present with extranodal involvement. The head and neck region represents one of the clinically relevant localizations. Sinonasal B-cell lymphomas are a rare subtype, most often manifesting as diffuse large B-cell lymphoma (DLBCL), and typically show aggressive

clinical behavior. Relapses most frequently involve cervical lymph nodes, the orbit, and the central nervous system. Ocular involvement is rare, usually presenting as orbital masses or ocular adnexal lymphoma. Vitreoretinal infiltration is even more unusual and has been described only infrequently. In this case report, we present an elderly male patient with nasal cavity B-cell lymphoma who developed relapse with vitreoretinal involvement, aiming to emphasize the diagnostic and therapeutic aspects of this rare condition. **Case Presentation:** A 71-year-old male was diagnosed three years earlier with nasal cavity B-cell lymphoma. Bone marrow biopsy at diagnosis showed no systemic involvement. He received four cycles of R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) and achieved complete remission. Three years later, he presented with decreased vision in the left eye. Orbital MRI showed tortuosity of the optic nerve and slight widening of the perioptic space (Figure 1). Cranial MRI revealed only age-related changes. Cytology and flow cytometry of vitreous fluid demonstrated CD20 and CD79a positivity with high proliferative activity, consistent with B-cell neoplasia. PET-CT revealed limited FDG uptake (SUVmax 5.02) in the anterior aspect of the left orbit (Figure 2), with no additional systemic involvement. Based on his disease history, systemic high-dose methotrexate combined with cytarabine and intrathecal therapy was initiated. Radiotherapy was also considered. He was referred to another specialized center for possible intravitreal chemotherapy. Despite systemic treatment, follow-up revealed that the patient had died. **Discussion and Conclusion:** Sinonasal B-cell lymphomas are uncommon, most often exhibiting DLBCL histology with aggressive clinical features. Relapses most frequently involve cervical nodes, orbital structures, or the central nervous system. Although orbital disease is recognized, vitreoretinal infiltration is exceedingly rare and has been reported in less than 5% of cases in large series. Diagnosis is challenging, as ocular involvement may present with non-specific symptoms such as visual impairment or vitreous opacities, requiring cytology, immunophenotyping, and immunohistochemistry of vitreous samples for confirmation. Therapeutic options include systemic high-dose methotrexate and cytarabine, with intrathecal therapy commonly added for central nervous system prophylaxis. Radiotherapy may contribute to local control in orbital disease. Intravitreal chemotherapy has also been described, most often with methotrexate, and rituximab has been used in selected cases. The prognosis of ocular involvement is poor, with median survival reported between 12 and 36 months and a high risk of central nervous system relapse. This case illustrates that vitreous infiltration may represent a relapse manifestation of sinonasal B-cell lymphoma and highlights the importance of careful evaluation of ocular symptoms in such patients.



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