LETTER TO THE EDITOR

Turk J Hematol 2025;42:227-229

Second Allogeneic Stem Cell Transplantation in an inv16 Patient with Acute Myeloid Leukemia and Isolated Central Nervous System Relapse in the Form of Pituitary Adenoma

Hipofiz Adenomu Şeklinde İzole Santral Sinir Sistemi Nüksü Olan inv16 Pozitif Akut Myeloid Lösemi Hastasında İkinci Allojenik Kök Hücre Nakli

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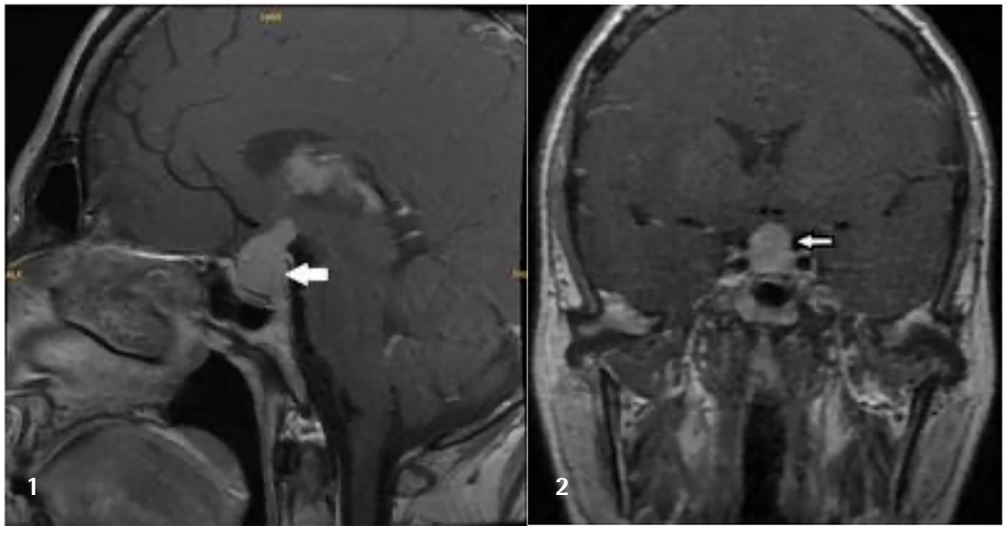
To the Editor,

It is uncommon for patients with acute myeloid leukemia (AML) to present with involvement of the central nervous system (CNS). We report a case of AML with CNS relapse after allogeneic stem cell transplantation (ASCT).

A 34-year-old man with AML M4-M5? with inversion 16 (inv16) and c-KIT positivity (standard risk) achieved complete remission with 3+7 (cytarabine and idarubicin). However, minimal residual disease (MRD) positivity was detected by flow cytometry at the end of consolidation treatment intermediate dose cytarabine regimen. Accordingly, ASCT was performed. The donor was a 36-year old HLA-matched female sibling. The patient underwent conditioning with a Cyclophosphamide-Busulfan (myeloablative regimen). In the second year after that transplantation, the patient presented with general malaise and headache. His adrenocorticotropic hormone (14 pg/mL; normal: <46), cortisol (2.1 µg/dL; normal: 5.2-22.4), thyroid-stimulating hormone (0.35 mIU/L; normal: 0.55-4.78), follicle-stimulating hormone (2.2 U/L; normal: 1.4-18.1), and luteinizing hormone (0.5 U/L; normal: 01.5-9.3) levels were found to be low with the possibility of Addison's disease. A magnetic resonance evaluation of the pituitary gland revealed the presence of a macroadenoma mass measuring 2.5x1.5 cm, which was observed to be occluding the suprasellar system and exerting a suppressive effect on the optic chiasm (Figures 1 and 2). Dexamethasone and thyroid hormone replacement were initiated for the management of Addison's disease. Cytological and flow cytometric evaluations of cerebrospinal fluid (CSF) were consistent with AML. Bone marrow biopsy was normocellular with MRD positivity.



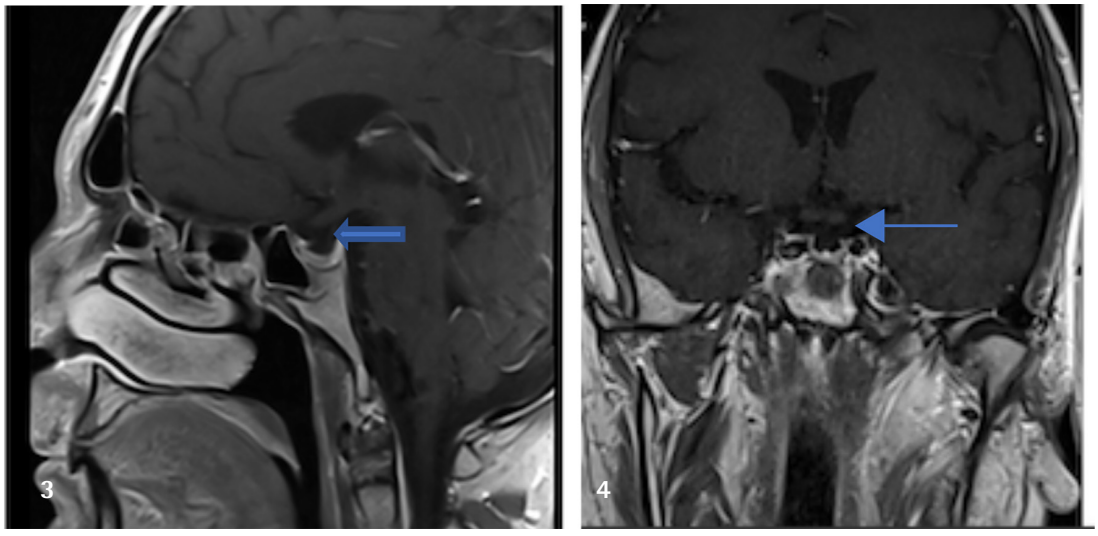
Figures 1 and 2. Brain magnetic resonance T2-weighted sequence showing occlusion of the suprasellar system with a suppressive effect on the optic chiasm.

Intrathecal treatment (weekly intrathecal cytarabine at 40 mg, methotrexate at 12 mg, and dexamethasone at 4 mg until negative results were obtained in the last two cytological evaluations) and radiotherapy (200 cGy per day for 12 days) were administered due to the isolated CNS involvement. Bone marrow biopsy re-evaluation due to cytopenia was consistent with disease recurrence. During this recurrence, chimerism was detected at a rate of 99.63%.

The patient was started on high-dose cytarabine and mitoxantrone. Bone marrow evaluation at the end of treatment showed 7%-8% blasts and MRD positivity. CSF cytology and testing for c-KIT and inv16 were also negative. He underwent ASCT again from the same donor with a myeloablative regimen including fludarabine and total body irradiation. An alternative non-sibling donor was not considered due to retrospective European Society for Blood and Marrow Transplantation (EBMT) analysis. In retrospective EBMT analysis, 2632 second allogeneic transplantations carried out for relapse after a first transplantation were analyzed to define indications and identify predictive factors [1]. This evaluation showed that using the same donor from the first transplantation had no predictive value for survival compared to the use of another donor. Sibling donors constituted a favorable predictive factor.

Our patient developed steroid resistance with acute skin graft-versus-host disease (MAGIC score: IV) on the 6th day after the transplant. A response was obtained with ruxolitinib. At 1 month after the second ASCT, CNS cytology was negative. No pathological findings were observed by cranial magnetic resonance imaging (Figures 3 and 4). A bone marrow evaluation yielded normocellular results and MRD positivity. The chimerism rate was 99.73%. Post-transplant azacytidine-donor lymphocyte infusion maintenance and intratechal prophylactic therapy were planned.

AML stages M4 and M5, the presence of inv16, chromosome 11 anomalies, hyperleukocytosis, lactate dehydrogenase elevation, and FLT3-internal tandem duplication mutations are risk factors related to CNS involvement of AML [2,3]. The findings indicate that CNS relapse following ASCT suggests a poor prognosis [4]. Once the disease has been successfully controlled, the subsequent step is to proceed with cellular therapy, such as a repeated ASCT [5]. Further prospective multicenter research is required to confirm these results and to investigate standard treatments for CNS relapse in AML patients following ASCT.



Figures 3 and 4. Brain magnetic resonance T2-weighted sequence showing a normal suprasellar system.

Keywords: Acute myeloid leukemia, Pituitary adenoma, Second allogeneic stem cell transplantation

Anahtar Sözcükler: Akut myeloid lösemi, Hipofiz adenomu, İkinci Allogeneik kök hücre nakli

Ethics

Informed Consent: Consent was obtained from the patient for the article.

Footnotes

Authorship Contributions

Concept: M.S.P.; Design: M.S.P.; Data Collection or Processing: M.S.P., F.Ö.; Analysis or Interpretation Literature Search: M.S.P., F.Ö.; Writing: M.S.P.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Received/Geliş tarihi: January 9, 2025
Accepted/Kabul tarihi: May 27, 2025

DOI: 10.4274/tjh.galenos.2025.2025.0011