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EDİTÖRE MEKTUP / LETTER TO THE EDITOR

Central nervous system involvement in acute graft versus host disease

Akut graft versus host hastalığında santral sinir sistemi tutulumu

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To the Editor,

Central nervous system (CNS) complications are rare in pediatric age group after allogenic hematopoietic stem cell transplantation (HSCT) comparing to adult counterparts who have an incidence of 9% to 14%[1]. Chronic graft-versus-host disease (GVHD) mainly targets liver, skin and intestine but may also involves other organs including CNS. It is unusual to encounter CNS involvement in the course of acute GVHD. In the present paper a 10-year-old girl with thalassemia major presenting with CNS complications in the course of acute GVHD after allogenic HSCT is reported.

The patient was a 10-year-old girl who received an allo-HSCT from one HLA-mismatched related donor (HLA-A mismatch) for thalassemia major. She had busulfan and cyclophosphamide as preparative regimen and was treated with cyclosporine and tacrolimus for GVHD prophylaxis. The patient developed grade III acute GVHD in skin, liver and intestine according to Glucksberg classification[2] on day 18 posttransplantation. On day 20, generalized tonic-clonic convulsions (2 times in a day) and agitation which were controlled by midazolam started. Magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) analysis showed no pathological findings. Electroencephalogram revealed normal brain activity. Serum biochemistry confirmed normal values for glucose and electrolytes. Blood, urine and CSF analysis also revealed no microbiological infection. She was treated with methylprednisolone in a dose of 2 mg/kg in addition to cyclosporine and tacrolimus. Skin rash and diarrhea of the patient improved in a week, whereas, hyperbilirubinemia continued for 20 days. Convulsions and agitation did not recur after day 20. Molecular analysis of lineage-specific chimerism revealed full donor chimerism.

In the course of acute GVHD, the reactions is initiated by donor T lymphocytes recognizing antigenic differences between the host and donor[3]. The classic target organs for acute GVHD are skin, liver and gastrointestinal tract. Maculopapular rash, liver function tests abnormalities and diarrhea are major clinical findings. Our patient had several risk factors for the development of GVHD including mismatched transplantation from the mother and peripheric stem cell transplantation. With a diagnosis of grade III acute GVHD, methylprednisolone therapy was added to the initial cyclosporine and tacrolimus. Convulsions were treated with antiepileptic drugs and agitation of the patient subsided.

In 2010, neurological manifestations of chronic GVHD were described as a distinct entity in the Consensus Conference on Clinical Practice in chronic GVHD. The Consensus Conference classified chronic CNS GVHD into three types; cerebrovascular disease, CNS demyelinating disease, and immune-mediated encephalitis[4]. However, there is no formal definition of acute CNS GVHD in the literature. In our case, there was no evidence of

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cerebrovascular disease on MRI. Similarly, white matter lesions consistent with demyelinating disease were not observed. CSF analysis also did not reveal any findings. In our case, although we are in doubt, there was no comment on immune-mediated encephalitis since no brain biopsy was performed. However, what is certain is that our patient's GVHD findings as well as CNS manifestations improved after immunosuppressive treatment.

In conclusion, although it is an unusual finding, clinicians should be aware of the CNS involvement during the course of acute GVHD. Although acute CNS GVHD is a rarely reported condition, CNS may be one of the affected organs in acute GVHD. Other causes of CNS disorders such as infections, drug side effects and involvement of the underlying disease should be investigated in detail tu rule out other possible etiologies.

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REFERENCES

1. Syed FI, Couriel DR, Frame D, Srinivasan A. Central nervous system complications of hematopoietic stem cell transplant. Hematol Oncol Clin North Am. 2016;30:887–98.
2. Glucksberg H, Storb R, Fefer A, Buckner CD, Neiman PE, Clift RA et al. Clinical manifestations of graft-versus-host disease in human recipients of marrow from HLA matched sibling donors. Transplantation 1974; 18: 295–304.
3. Choi SW, Levine JE, Ferrara JL. Pathogenesis and management of graft-versus-host disease. Immunol Allergy Clin North Am. 2010;30:75-101.
4. Grauer O, Wolff D, Bertz H, Greinix H, Kühl JS, Lawitschka A et al. Neurological manifestations of chronic graft-versus-host disease after allogeneic haematopoietic stem cell transplantation: report from the Consensus Conference on Clinical Practice in chronic graftversus-host disease. Brain. 2010;133:2852–65.