

Accidental High-dose Intrathecal Treatment: Late Results of a Patient

Yanlışlıkla Uygulanan Yüksek Doz Metotreksat: Bir Hastada Geç Sonuçlar

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To the Editor,

The increase in reporting accidental and overdose use of childhood treatments, starting from 2014, is promising. Understanding the dynamics of overdose may help in the development of more effective prevention and control strategies [1]. Herein, we want to share one of our patients with an overdose of intrathecal treatment.

The survival rates of patients with leukemia and lymphoma have improved after prophylactic intrathecal methotrexate treatments. There have also been some case reports about the mortality or morbidity of intrathecal methotrexate or folinic acid [2,3,4,5,6,7,8,9]. We experienced a nursing error in which 35 mg of intrathecal methotrexate was administered instead of the planned 12 mg to a 3-year-old boy with T-cell non-Hodgkin lymphoma, stage IV. The patient was receiving the first day of the regimen of the second cytarabine block of protocol I, phase 2, BFM (Berlin-Frankfurt-Münster). The error was recognized after about 60 minutes. We performed neither CSF drainage nor exchange as Kazancı et al. [9] had done for their two patients. We thought of intrathecal folinic acid administration, but there were no data about its intrathecal use. Carboxypeptidase G2 was not available in our country. We administered 9 mg of folinic acid (15 mg/m²) intravenously, followed by 100 mg of folinic acid (150 mg/m²) infused in 6 hours. The patient was monitored for toxic signs and symptoms. He developed no clinical signs. Cranial computed tomography (CT) performed 2 days after the incident revealed no morphological changes. He was followed after this accident for 15 years. Although his neurological development was normal and his most recent cranial CT and electroencephalography results revealed no sequelae, he has had two unsuccessful suicide attempts.

If a readily available source of information regarding the action needed to be taken after such an incident had been available, we could have approached the child more comfortably and confidently, and our colleagues who used intrathecal folinic acid would not have done so [4]. As methotrexate doses of up to 500 mg have not been

associated with untoward events, deciding when to hold an intervention is important.

Keywords: Overdose, Intrathecal methotrexate, Folinic acid

Anahtar Sözcükler: Yüksek doz, İntratekal metotreksat, Folinik asit

Informed Consent: Written informed consent was obtained.

Authorship Contributions

Surgical and Medical Practices: T.C.; Concept: T.C.; Design: E.Ç.S.; Data Collection or Processing: E.Ç.S., T.C.; Analysis or Interpretation: T.C.; Literature Search: E.Ç.S.; Writing: T.C.

Conflict of Interest: The authors declare that there is no conflict of interest.

Financial Disclosure: There is no financial conflict of interest to declare.

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Turkish Journal of Hematology, Published by Galenos Publishing House

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Received/Geliş tarihi: July 25, 2019
Accepted/Kabul tarihi: September 16, 2019

DOI: 10.4274/tjh.galenos.2019.2019.0283

CMV-specific T-Cells for Treatment of CMV Infection after Hematopoietic Stem Cell Transplantation in a Pediatric Case: First Application in Turkey

Pediyatrik Bir Olguda HKHN Sonrası CMV Spesifik T Hücre Kullanımı: Türkiye'deki İlk Uygulama

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To the Editor,

Cytomegalovirus (CMV) infection is still a major complication after allogeneic hematopoietic stem cell transplantation (HSCT) [1,2]. Unfortunately, prolonged antiviral treatment of CMV infection causes a delayed CMV-specific immune reconstitution. At this point, adoptive immunotherapy by CMV-specific T-cells can control CMV infection or provide immune reconstruction [3,4,5].

A 17-year-old boy with high-risk T-cell acute lymphoblastic leukemia underwent HSCT from one antigen-mismatched unrelated donor. He was conditioned with treosulfan, fludarabine, thiopeta, and rabbit anti-thymocyte globulin at 15 g/m² for 3 consecutive days (days -2 to 0). The patient also received cyclosporine A (CsA) divided into two doses: 3 mg/kg daily from day -1 to post-transplant days +20 and +30 intravenously then switched to approximately 6 mg/kg peroral daily (targeted blood concentration: 200-250 ng/mL with monitoring). CsA was tapered quickly and stopped in the third month of transplant due to renal failure. Methotrexate was administered on days +1 (10 mg/m²), +3 (8 mg/m²), and +6 (8 mg/m²). He achieved neutrophil engraftment on day +17 and thrombocyte engraftment on day +32. Full donor chimerism was observed in the first and third months. Lymphoid engraftment was achieved on day +75 but generally the absolute lymphocyte

count was under 1500/mm³. He was CMV immunoglobulin G (IgG)-seropositive and CMV-DNA polymerase chain reaction (PCR) was negative before transplantation. Unfortunately, his donor was CMV IgG-seronegative. CMV infection (reactivation) occurred on day +19. Ganciclovir was started at 10 mg/kg/day and no response was obtained in 14 days. CMV drug resistance mutation was detected in the *UL54* polymerase gene. Foscarnet was administered at 180 mg/kg/day on day +34. First, an increase of CD3+ lymphocytes was seen in the lymphocyte subtype analyses around the third month after the transplant. As a comorbidity, in spite of the fact that fluoroquinolone was administered until +30 day, BK virus infection developed in the patient and cidofovir was used at 5 mg/kg/week on days +52, +67, and +79. No response was achieved with the antiviral treatment and renal failure developed in the patient on day +82. All antivirals were stopped. According to the recent literature, the transplant council decided to use CMV-specific T-cells for the patient's ongoing CMV infection. Informed consent was received from his family and the application was approved by the Ministry of Health's Scientific Advisory Commission on Stem Cell Transplantation. In accordance with cGMP standards, peptide-specific T lymphocytes were isolated and amplified by a interferon- γ cytokine capture system using the fully automated CliniMACS Prodigy device at Acibadem Labcell, İstanbul. The