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SHORT REPORT

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Successful engraftment and decrease of cytomegalovirus load after cord blood stem cell transplantation in a patient with DiGeorge syndrome

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A patient with DiGeorge syndrome showed a decrease of cytomegalovirus load after cord blood stem cell transplantation.

A 3-month-old infant was admitted to hospital because of prolonged seizures. He was born at 37 weeks and 2 days gestation with a birth weight of 1864 g. He showed a significant decrease in serum Ca^{2+}, Na^{+} and Cl^{-} levels, with inappropriate ADH secretion, and was treated with water restriction and Ca^{2+} supplementation. Several minor anomalies, such as low-set ears, small-sized jaw, muscle hypotonia, retarded development and growth of body weight 4260 g (-3.0 SD) and body length 54 cm (–3 SD), and absence of thymus, genital hypoplasia, together with hypoparathyroidism (intact PTH <9 pg/ml), and lack of T-cells (5 cells/μl) led to a diagnosis of DiGeorge syndrome on day 100.

The boy suffered from persistent fever, diarrhoea, and cough, with interstitial pneumonia, gastroenteritis, hepatitis, and retinopathy. Both cytomegalovirus (CMV) antigen and CMV-DNA were detected in blood and urine samples, suggestive of systemic CMV infection. He was treated with ganciclovir, γ-globulin with high titres of CMV-IgG, and foscarnet sodium hydrate. The CMV load decreased from 60,000 genome copies/10 μl whole blood to 12,000, but no lower, and the symptoms such as fever, diarrhoea, and cough persisted (Table 1). Cord blood stem cell transplantation (CBSCT) was performed by infusion of 10.3×10^{8} cord blood stem cells without preconditioning and with the use of cyclosporine (5 mg/kg per day) on day 220 (Table 1). Within 20 days after the CBSCT, his general condition, i.e. fever, cough, and general activities improved and a significant increase in T-cells (1690/μl) with dramatic reduction of CMV to 1000 copies was observed without any serious complications. However, respiratory distress and diarrhoea worsened gradually with a relapse of CMV infection up to 11,000 copies after the use of corticosteroids resulting in death on day 253.

CMV infection is a fatal complication in T-cell deficient patients. CBSCT is an ideal treatment for introducing T-cell immunity, since premature T-cells do not induce serious graft-versus-host disease (GvHD) in the immune deficient host [1]. The reduction in CMV-DNA copies from 12,000/10 μl whole blood to 1,000 with increased T-cell counts suggests that CBSCT is effective for the treatment of CMV infection in DiGeorge syndrome.

Although CBSCT successfully reduced the number of CMV-DNA copies, the respiratory distress and intestinal bleeding progressed. We cannot exclude the possibility that the introduction of lymphocytes accelerated the development of inflammation in the host organ. We do not suspect that these symptoms were caused by GvHD but possibly by systemic CMV disease, since the high CMV load was observed after CBSCT without any typical GvHD symptoms, i.e. skin lesions and liver dysfunction. Corticosteroid

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Table 1 Treatment schedule in an attempt to eradicate CMV-load

Day 78	100		160				220		240	253
γ-globulin	↓	↓	↓	↓	↓	↓	↓	↓	↓	
Ganciclovir (10 mg/kg/day) (5 mg/kg/day)	→									
Foscarnet (180 mg/kg/day) (120 mg/kg/day)			→							
CBSCT							↓			
CMV-DNA (copies/10μl whole blood)			30,000	28,000	64,000		12,000	1,000	10,000	11,000
WBC	19900 /μl									
Neutrophil	17900 (90.0 %)									
Lymphocyte	1690 (8.5 %)									
$CD3^+$	5 (0.3 %)							1,690	572	182
$CD19^+$	870 (51.3 %)									
Na^+	119 mEq/L	142								
Cl^-	84 mEq/L	102								
Ca^{2+}	4.8 mg/dl	9.1	10.2							
ALPase	1896 IU/L	1154	698							
intact PTH (> 9 pg/ml)	3 pg/ml	3	3							

therapy was necessary for control of the interstitial pneumonia. Moreover, administration of immunosuppressants resulted in T-cell proliferation which might have led to a more active CMV disease. Our limited experience suggests that CBSCT was successful in reducing the CMV load, but should have been performed before the development of systemic chronic CMV infection.

Reference

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