Cellular Therapy and Transplantation (CTT), Vol. 2, No. 5, 2009
doi: 10.3205/ctt-2009-No5-abstract58

Abstract accepted for "Joint EBMT Pediatric Working Party – 3rd Raisa Gorbacheva Memorial Meeting on Hematopoietic Stem Cell Transplantation", Saint Petersburg, Russia, September 17–20, 2009

Management of resistant or recurrent CMV infection following allogeneic SCT

Petr Sedlacek[1], Ladislav Krol[1], Petr Hubacek[1], David Boutolleau[2], Tomas Kalina[1]

[1]Department of Pediatric Hematology and Oncology, HSCT Unit, Prague, Czech Republic;
[2]UPMC University Paris and Service de Virologie, GH Pitié-Salpêtrière, Paris, France

Correspondence: Prof. Petr Sedlacek, MD, PhD, Department of Pediatric Hematology and Oncology, HSCT Unit – Head, University Hospital Motol, 2nd Medical School, Charles University in Prague, V Uvalu 84, 150 06, Prague, Czech Republic, Phone: +42 (02) 2443-6552, Fax: +42 (02) 2443-6519, E-mail: petr.sedlacek@lfmotol.cuni.cz

Abstract

Despite the strategy of preemptive treatment of CMV infections, CMV disease is still a major cause of morbidity and mortality after allogeneic hematopoietic stem cell transplantation. Patients who failed to respond to ganciclovir (GCV) may be rescued by other virostatics or by cellular therapy. Conversely, by using preemptive strategies a lot of patients might be unnecessarily overtreated. Other tools have to be exploited in order to improve post–transplant management of CMV infection.

We monitor CMV quantity in whole blood using real-time PCR technology. If resistance to GCV is suspected, we change the therapy and we indicate PCR detection of the most frequent CMV resistant strains. Detection of CMV-specific immune response is based on a polychromatic flow cytometry cytokine staining method. We evaluate the ability of CD4+ and CD8+ T-cells to produce interferon-γ and interleukin-2, to express activation marker CD40L, and/or to mobilize degranulation marker CD107a in response to CMV antigens.

In almost half of about 200 pediatric patients we detected CMV DNA in the sample; about 30% of them were indicated for preemptive therapy. Despite preemptive therapy CMV disease developed in 10 children (8 deceased). Clinical suspicion for CMV resistant strains was observed in 22 children and known resistance mutation was proved in 4 of them.

Implementation of methods that allow CMV-specific T-cell reconstitution monitoring may allow us to define a subgroup of patients who are able to resolve a CMV infection without virostatics. These patients could be spared from virostatic toxicity. Inefficient reconstitution of immunity, infection with ganciclovir resistant CMV strains, and inadequate intensity of therapy are factors responsible for treatment failure.

Acknowledgements: Supported by GAUK-47807/2007, IGA ČR -NS/9996-4 and NR/9418-3.

Keywords: CMV disease, allogeneic stem cell transplantation, resistance, reconstitution of immunity, PCR monitoring