*Letter to the Editor*

# Cytomegalovirus infection in patients undergoing autologous peripheral blood stem cell transplantation

Massimo Franchini,[1] Sergio Pizzighella,[2] Aurora Vassanelli,[1] Paolo Rocca,[1] Vittorio Meneghini,[1] Dino Veneri,[1] Giuseppe Lippi[3] and Fabio Benedetti[1]

Cytomegalovirus (CMV) infection is a well known cause of morbidity and mortality in patients undergoing allogeneic bone marrow transplantation (BMT) management. Although many clinical trials have been carried out worldwide on this topic,[1] little is known about the role of CMV infection after autologous BMT (ABMT).[2–5]

In this study, the incidence and the clinical characteristics of CMV infection were evaluated in 40 consecutive patients (29 male and 11 female; mean age 40 y, range 28–59 y) affected by hematologic malignancies. The subjects were enrolled between January 1995 and December 1998 in a sequential high-dose chemotherapy program with peripheral blood stem cell (PBSC) rescue. Twenty-two patients had non-Hodgkin's lymphoma, twelve had Hodgkin's disease, and six had multiple myeloma. The high-dose chemotherapy regimen included cyclophosphamide 7000 mg/m$^2$ intravenously (IV) on day −48 followed by granulocyte-macrophage colony-stimulating factor (GM-CSF) 5 μg/kg IV once daily until PBSC collection. Methotrexate 8000 mg/m$^2$ IV with leucovorin rescue and vincristine 1.4 mg/m$^2$ IV were given on day −28. Etoposide 2000 mg/m$^2$ IV was given on day −20 followed by granulocyte colony-stimulating factor (G-CSF) (5 μg/kg/d IV) starting on day −19 until the absolute neutrophil count was above $0.5\times10^9$/L for 3 consecutive days. Patients received melphalan (140 mg/m$^2$ IV) and mitoxantrone (60 mg/m$^2$ IV) on day −2 and PBSC were infused on day 0. Granulocyte CSF (5 μg/kg/IV once daily) was given starting on day +1 until the absolute neutrophil count was above $0.5\times10^9$/L for 3 consecutive days. Thirty-three of 40 patients (82.5%) were CMV positive (IgG+, IgM−) at the time of transplantation. All patients enrolled were tested weekly for CMV pp65 antigenemia, with shell vials and long-term cultures starting before the chemotherapy regimen and continuing until the patient was discharged. Twenty-three patients (57.5%) received CMV prophylaxis with acyclovir 10 mg/kg IV three times a day starting on day −5 through day +30 after transplantion. Cytomegalovirus infection developed in 11 of 40 patients (27.5%), all but one without CMV prophylaxis. Nine of eleven patients (81.8%) were CMV IgG positive (CMV reactivation), two (18.2%) were CMV IgG negative (primary infection). In all 11 cases, infection was defined by an antigenemia-positive test. Positive shell vials and long-term cultures from blood were detected in five of eleven patients (45.4%). Positive cultures from urine

**Table 1.** Summary of Clinical and Therapeutic Data

| Patient number | Disease | CMV status at ABMT (IgG) | CMV prophylaxis (Acyclovir) | Antigenemia (Ag pp65 x $10^6$) | Viremia | | Viruria | | Therapy |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | SV | LTC | SV | LTC | |
| 1 | HD | − | No | 1500 | + | + | + | + | Acyclovir+Foscavir |
| 2 | NHL | + | No | 2 | + | + | + | + | Acyclovir |
| 3 | HD | + | No | 2 | − | − | − | − | Acyclovir |
| 4 | MM | + | No | 3 | − | − | − | − | Acyclovir |
| 5 | MM | + | No | 5 | − | − | + | + | Acyclovir |
| 6 | MM | + | No | 10 | − | − | + | + | Ayclovir+Ganciclovir |
| 7 | HD | + | No | 700 | + | + | + | + | Acyclovir |
| 8 | NHL | + | No | 10 | − | − | − | − | Acyclovir |
| 9 | NHL | + | Yes | 4 | − | − | − | − | Acyclovir |
| 10 | HD | − | No | 12 | + | + | + | + | Acyclovir+Foscavir |
| 11 | HD | + | No | 750 | + | + | + | + | Acyclovir+Foscavir |

HD=Hodgkin's disease; NHL=non-Hodgkin's lymphoma; MM=multiple myeloma; CMV=cytomegalovirus; ABMT=autologous bone marrow transplantation; SV=shell vial; LTC=long-term culture; −=negative; +=positive.

[1]Dipartimento di Medicina Clinica e Sperimentale, Sezione di Ematologia, Università di Verona; [2]Laboratorio di Microbiologia, Ospedale Civile Maggiore, Verona; [3]Istituto di Chimica e Microscopia Clinica, Dipartimento di Scienze Biomediche e Morfologiche, Università di Verona, Verona, Italy.

Address correspondence to Dr. Massimo Franchini, Servizio di Immunoematologia e Trasfusione, Ospedale Policlinico, 37134 Verona, Italy. E-mail;mfranchini1@hotmail.com

**Corresponding Editorial Office: New York**

were detected in seven of eleven patients (63.6%): viruria without viremia was noted in two cases (patients 5 and 6). In most cases, infection occurred just prior to autologous PBSC transplantation (average time, 3 d before transplantation; range −21 d pre-BMT, +20 d post-BMT). The patients' characteristics, the CMV status at transplantation, the CMV monitoring, and the therapeutic data are summarized in Table 1. In all cases, CMV infection was only a laboratory finding and none of the patients had clinical symptoms. Treatment with acyclovir 15 mg/kg IV three times a day rapidly resolved the infection in seven of eleven patients, whereas four patients (all without prophylaxis) required further therapy with ganciclovir or foscarnet.

The data show that patients undergoing high-dose chemotherapy regimens may be at risk for CMV reactivation. Although CMV reactivation was only a laboratory finding in these patients undergoing autologous PBSC transplantation, this report underlines the need for close monitoring for CMV following BMT.

## REFERENCES

1. Zaia JA. Cytomegalovirus infection. In: Forman SJ, Blume KG, Thomas ED, eds. Bone marrow transplantation. Boston: Blackwell Scientific Publications 1994:376–403.
2. Wingard JR, Chen DY, Burns WH, et al. Cytomegalovirus infection after autologous bone marrow transplantation with comparison to infection after allogeneic bone marrow transplantation. Blood 1988; 71:1432–1437.
3. Reusser P, Fisher LD, Buckner CD, Thomas ED, Meyers JD. Cytomegalovirus infection after autologus bone marrow transplantation: occurrence of cytomegalovirus disease and effect on engraftment. Blood 1990; 75: 1888–1894.
4. Hebart H, Schröder A, Löffler J, et al. Cytomegalovirus monitoring by polymerase chain reaction of whole blood samples from patients undergoing autologous bone marrow or peripheral blood progenitor cell transplantation. J Infect Dis 1997; 175:1490–1493.
5. Boeckh M, Stevens-Ayers T, Bowden RA. Cytomegalovirus pp65 antigenemia after autologous marrow and peripheral blood stem cell transplantation. J Infect Dis 1996; 174:907–912.