Objective: To explore the risk factors and prophylaxis and treatment of cytomegalovirus interstitial pneumonitis (CMV-IP) after allogeneic peripheral blood stem cell transplantation (allo-PBSCT). Methods: 43 patients who received allo-PBSCT were allocated to either a Gancyclovir (GCV)-prophylaxis group (n=19) or a non-GCV prophylaxis group (n=24). A comparison was made of the incidence of CMV-IP in patients given or not given prophylactic gancyclovir. Results: 9 patients in non-GCV prophylaxis group developed late CMV-IP (P<0.05). Graft-versus-host-disease (GVHD) may be associated with a high risk of CMV-IP. 5 cases of CMV-IP were successfully treated with GCV, but 3 cases died of CMV-IP. The most common adverse event of GCV was neutropenia, but was reversible. Conclusion: CMV infection was a major cause of interstitial pneumonitis after allo-PBSCT, which correlated strongly with the severity of GVHD. Gancyclovir was shown to be effective in both prophylaxis and treatment of CMV-IP.

Key words: Allogeneic; Peripheral blood stem cell transplantation; Interstitial pneumonitis; Cytomegalovirus; Graft-Versus-Host-Disease

Cytomegalovirus interstitial pneumonia (CMV-IP) is a very important and common complication of hematopoietic stem cell transplantation (HSCT), which can influence the outcome of this procedure[1]. The high incidence of cytomegalovirus infection and disease in recipients of bone marrow allograft and the 85% mortality rate associated with cytomegalovirus pneumonia make this disease the leading infectious cause of death after HSCT[2]. In the present study, we analyzed the incidence and treatment of CMV-IP in 43 consecutive allogeneic peripheral blood stem cell transplantations (allo-PBSCT) performed at our department.

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MATERIALS AND METHODS

Patients

The subjects were 43 patients including 26 men and 17 women who underwent allo-PBSCT at our department between June 1997 and November 2004. Their age ranged from 23 to 48 years (median age 34). Patients with chronic myeloid leukemia (CML) were transplanted in the chronic phase (19 cases) and blast crisis (2 cases), patients with acute myeloid leukemia (AML) were transplanted in first complete remission (CR, 16 patients), patients with acute lymphocytic leukemia (ALL) were transplanted in first CR (6 patients).

Donors

Forty-two patients received PBSC from HLA-identical sibling donors and the remaining one from haploidentical related donor. 16 donors were men and 27 were women with donor-recipient sex mismatch
in 21 patients. Their median age was 35 years (range 21 to 52 years). A major ABO-mismatch was present in 15 donor-recipient pairs.

Methods

PBSC mobilization and collections

Donors PBSCs were mobilized into the peripheral blood using subcutaneous injection of glycosylated rhG-CSF at a dose of 5 μg/kg every 12 hours for 5–6 days. PBSCs were collected using the CS 3000 plus blood cell separator. A total of 10–12 liters of whole blood was processed per apheresis. PBSCs were infused immediately after collection and on days 0 + 1.

Conditioning regimen

Busulphan and cyclophosphamide (Bu-Cy) were used as the conditioning regimen for all patients following the procedure. Busulphan 1 mg/kg po. Every 6 hours for 4 consecutive days followed by cyclophosphamide 60 mg/kg iv. for 2 consecutive days.

CMV-IP prophylaxis

Forty-three patients who received allo-PBSCT were allocated to ganciclovir (GCV) group (n=19) and no GCV prophylaxis group (n=24). GCV prophylaxis group patients received intravenous GCV at a dose of 5 mg/kg every other day for +30 to +90 days.

Laboratory methods

Antibody to CMV was measured by an enzyme linked immunoabsorbent assay (ELISA) for IgG and IgM antibody. CMV antibody was measured in donors and recipients before transplantation. 14 patients were CMV-IgG positive, 15 donors were CMV-IgG positive (Table 1), none of them was CMV-IgM positive, 9 patients in non-GCV prophylaxis group receiving allo-PBSCT had CMV infection, 7 patients developed CMV-IP, 2 antigenemia, while only one patients in GCV-prophylaxis group developed late CMV-IP (P<0.05). CMV-IP occurred in 7 patients in no GCV prophylaxis group, defined as an interstitial infiltrate recognized on chest radiographs. CMV-IP occurred at a median of 57 days (range 42 to 296 days) after transplant, and treatment was started at a median of 3 days (range 1 to 9 days) later. Patients received a median of 14 days (range 3 to 32 days) GCV therapy. Only one patient in GCV prophylaxis group occurred CMV-IP 1153 days after transplantation.

GVHD prophylaxis

Cyclosporine A (CsA) and methylprednisolone (MP) were used for GVHD prophylaxis in 6 patients. CsA and methotrexate (MTX) were used in 37 patients. CsA was initiated on day-1 at 3 mg/kg/d intravenously by continuous infusion and the dose was adjusted to maintain a whole blood radio-immunoassay level of 200 to 400 ng/ml. MP was administered at a dose of 15 mg/m² on day +1 and 10 mg/m² on days +3 and +6.

Statistical analysis

Statistical analysis was done using the Fishers Exact test, and P<0.05 was considered to indicate a significant difference.

RESULTS

Clinical Outcome

Forty-three patients who received allo-PBSCT were allocated to ganciclovir (GCV) group (n=19) and no GCV prophylaxis group (n=24) (Table 1). CMV antibody was measured by ELISA for IgG and IgM antibody in donors and recipients before transplantation. 14 patients were CMV-IgG positive, 15 donors were CMV-IgG positive (Table 1), none of them was CMV-IgM positive, 9 patients in non-GCV prophylaxis group receiving allo-PBSCT had CMV infection, 7 patients developed CMV-IP, 2 antigenemia, while only one patients in GCV-prophylaxis group developed late CMV-IP (P<0.05). CMV-IP occurred in 7 patients in no GCV prophylaxis group, defined as an interstitial infiltrate recognized on chest radiographs. CMV-IP occurred at a median of 57 days (range 42 to 296 days) after transplant, and treatment was started at a median of 3 days (range 1 to 9 days) later. Patients received a median of 14 days (range 3 to 32 days) GCV therapy. Only one patient in GCV prophylaxis group occurred CMV-IP 1153 days after transplantation.

GVHD

The occurrence of acute GVHD was associated with the development of CMV antigenemia (P<0.05). Acute GVHD occurred in 18 of 42 patients receiving PBSC from HLA-identical sibling donors (42.85%), grade I-II in 16 patients and grade IV in 2 patients, in one receiving