Long-Term Remission of Chronic Myelogenous Leukaemia following Allogeneic Transplantation of Peripheral Blood Progenitor Cells in the Fourth Chronic Phase after Failing Previous Bone Marrow Transplantation and Donor Leukocyte Transfusion

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Allogeneic bone marrow transplantation (BMT) is the only curative option for chronic myelogenous leukaemia (CML) [1]. However, the relapse rates in patients transplanted for CML in the first chronic phase (CP) vary from 10 to 20% in recipients of non-T-cell-depleted allografts [1]. Management of CML patients relapsing after BMT is difficult: (1) Conventional chemotherapy offers little prospect of prolonging survival; (2) interferon induces cytogenetic remission in only a minority of patients; (3) a second BMT carries a high morbidity and mortality risk [2], and (4) immunotherapy by infusion of leukocytes from the same donor has been shown to be effective, but not always applicable or successful [3].

We report the case of a 20-year-old white woman with CML in the first CP diagnosed in September 1988 (fig. 1). After treatment with hydroxyurea for 2 years, she received an allogeneic BMT in August 1990 (donor: HLA-identical mother) following myeloablative therapy consisting of total body irradiation and cyclophosphamide. The patient had prompt haematopoietic engraftment after 23 days and neither acute nor chronic graft-versus-host disease (GvHD). She remained disease-free until July 1993, when haematological relapse into the second CP occurred followed by myeloid blast crisis (BC) in November 1993. After chemotherapy (daunorubicin and cytosine-arabioside) and achievement of a third CP in January 1994, she received three transfusions of peripheral blood mononuclear cells (donor leukocyte transfusion) from her mother. Subsequent treatment with interferon-alfa had to be discontinued due to adverse reactions (severe flu-like symptoms). In August 1994, the patient experienced a second myeloid blast crisis and was successfully reinduced into a fourth CP with chemotherapy (carboplatinum, idarubicin, and cytosine-arabioside). In order to consolidate treatment with a curative intention, the patient received a second allogeneic transplantation. After myeloablative therapy with busulfan and cyclophosphamide, she was transplanted with

allogeneic peripheral blood progenitor cells (PBPC) (three leukapheresis products) from the original donor who had been treated with recombinant human granulocyte-colony-stimulating factor (rhG-CSF) to mobilize haematopoietic stem/progenitor cells into the peripheral blood. No GvHD prophylaxis was given in order to take advantage of a possible graft-versus-leukaemia (GvL) effect which has been shown to be operative in CML [3]. Haematopoietic engraftment occurred 12 days after the first PBPC infusion. The patient developed acute GvHD grade II (skin and liver), which resolved upon steroid treatment, and chronic GvHD (skin, liver, thrombocytopenia) responsive to steroids and cyclosporine. The patient has remained disease-free and well for 17 months after the second allogeneic PBPC transplantation. Determination of haematopoietic chimerism has shown full sustained donor haematopoiesis until now. The 6-year probability of survival for CML patients relapsing in chronic phase after allogeneic BMT has been reported to be approximately 30% [2]. For patients with no contraindications such as active or prior history of severe acute GvHD, moderate or severe chronic GvHD, donor buffy coat infusion might be considered the treatment of choice [3]. However, for CML patients failing this adoptive immunotherapy, a second BMT may offer the

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BMT

DLT

PBPCT

4th CP

9/94

Fig. 1. Disease course. CP = Chronic phase; BC = blast crisis; BMT = bone marrow transplantation; DLT = donor leukocyte transfusion; PBPCT = peripheral blood progenitor cell transplantation; FDH = full donor haematopoiesis.

1st CP

9/88 8/90

Relapse

2nd CP

1

7/93

1st BC

11/93 1/94

2nd BC

3rd CP

8/94

FDH

2/96

only chance of cure. Considering both the different graft composition (higher T and NK cells) and the accelerated haematopoietic recovery kinetics [4, 5], allogeneic transplantation of PBPC might be advantageous because of its higher potential GvL effect and less transplant-related

morbidity and mortality compared to a second BMT. In conclusion, allogeneic PBPC transplantation offers an attractive treatment option for CML patients relapsing after BMT and failing or being ineligible for donor leukocyte infusions.

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Allogeneic PBPC in CML

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