

The Inefficacy of Micro-transplantation in a Patient with Relapsed Acute Lymphocytic Leukaemia

The Editor

Sir,

Treating adult patients with relapsed acute lymphocytic leukaemia (ALL) is still difficult. Only 20 % to 30% of those patients acquired complete remission (CR) which is always of short duration unless an allogeneic haematopoietic stem cell transplant (allo-HSCT) is feasible (1–3). But Allo-HSCT with intensive myeloablative conditioning results in a higher relapse rate in patients with relapsed ALL, higher severe graft-versus-host disease (GVHD) and transplantation-related mortality. Therapeutic strategy on relapsed ALL is always a major therapeutic challenge bothering haematological researchers (4, 5). Recently, two clinical studies demonstrated that infusion of HLA-mismatched granulocyte colony-stimulating factor (G-CSF)-mobilized donor peripheral-blood stem cells (GPBSC) and combined with chemotherapy, improves elderly patients with acute myeloid leukaemia (AML) outcome and avoids GVHD (6, 7). However, the clinical use of infusion of HLA-mismatched GPBSC has not been reported so far in relapsed/refractory ALL. We present the first micro-transplantation induction therapy in a patient with twice relapsed ALL.

A 31-year-old man was diagnosed in May 2013 with common B-cell ALL by bone marrow puncture. Complete blood count showed white blood cells (WBC) $64 \times 10^9/L$ (80% blasts), haemoglobin 124 g/L and platelets $43 \times 10^9/L$. Structural karyotype was normal. Acute lymphocytic leukaemia was negative for BCR-ABL or TEL-AML1 translocations and MLL rearrangements in molecular studies.

Acute lymphocytic leukaemia was classified into standard risk, and treated with vincristine, prednisone, daunomycin, L-asparaginase and cyclophosphamide as induction therapy. The patient did not achieve response. Then the patient was treated with hyper cyclophosphamide, dexamethasone, epirubicin, vindesine (CVAD) as salvage therapy. The patient still did not achieve response. The patient was then treated with Fludarabine, Ara-c, G-CSF (FLAG) and achieved complete remission. However, the disease relapsed after consolidation

by FLAG. Then the patient received chemotherapy with Fludarabine 30 mg/m² qd d1, MTX 1.5 g/m² qd d1, Ara-c 1g/m² q12h d2-3, respective HLA-mismatched G-PBSCs were administered 36 hours after the administration of cytarabine. The numbers of mononuclear, CD34+ cells and natural killer (NK) cells were $5.5 \times 10^8/kg$, $2.25 \times 10^6/kg$ and $0.36 \times 10^8/kg$, respectively. However, the patient did not achieve any response to the therapy once again and died ultimately from gastrointestinal haemorrhage two months later.

Guo *et al* suggested that regimens, such as fludarabine and TBI that possess stronger immunosuppressive effects, should be used with caution in infusion of GPBSC in order to prevent GVHD (6, 7). In this case, we found fludarabine may also be safe in microtransplantation.

Guo *et al* suggested that NK cells contributed to the antileukemic effects and improved clinical outcome (6, 7). In this patient, many more NK cells were infused but showed poor antileukemic effects. To our knowledge, this is the first case using HLA-mismatched granulocyte colony-stimulating factor-mobilized donor peripheral blood stem cell (GPBSC) in a patient with relapsed ALL. However, the case has shown that the combination of HLA-mismatched G-PBSC infusion with immunosuppressive treatment failed to induce CR in relapsed ALL. More clinical trials, are needed.

Keywords: Microtransplantation, relapsed acute lymphocytic leukemia, therapy

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