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Bone Marrow Transplant for Acute Leukaemia in Childhood : Experience in Singapore.

P. Han, C. Quah, R. Suri and H. B. Wong

Haematology Division Laboratory Medicine
Dept of Paediatrics and Dept of Medicine
National University Hospital, Singapore

The percentage of long term leukaemia-free survival in "good prognosis" childhood acute leukaemia is at least 50% [1]. The cure rate for the high risk acute lymphoblastic leukaemia (ALL) and acute non-lymphoblastic leukaemia (ANLL) is poorless than 20% [2]. Experience to date indicates that bone marrow transplant (BMT) is an acceptable mode of curative therapy for acute leukaemia [3-4]. BMT allows two potential therapeutic advantages over standard therapy. One, it allows high intense chemotherapy for cytoreduction of leukaemic cells as infusion of marrow "rescues" the patient from a potentially lethal therapy. Secondly, the graft-versus-host effect post-transplant may provide an immune effect against residual leukaemic cells. The best results of BMT were in patients transplanted with histocompatible allogeneic bone marrow and in first remission [5]. In Singapore, we have initiated a transplant program and five children had been transplanted for curative therapy of their acute leukaemia or CML.

The demographic and clinical data of these children are given in Table 1. They were 15 years and younger and underwent BMT for ALL, ANLL or CML in blast crisis (BC). Two of them were given syngeneic marrow and the rest HLA-matched and MLR non-reactive allogeneic marrow. The patients were prepared for allogeneic or syngeneic BMT with cyclophosphamide (CY), 50mg／kg／d on each of two consecutive days starting day－5 (Fig. 1).This was followed by fractionated total body irradiation (TBI) delivered at 20Gy／fraction over three days. The child with CML in BC was given high dose busulphan (4mg／kg／d) on each consecutive 4 days instead of TBI and followed by 4 days of CY 50mg／kg／d. Except for the first two transplants, subsequent BMT patients were given mesna as prophylaxis against haemorrhagic cystitis. The last three patients were given high dose intravenous immunoglobulin containing high titre antibodies against CMV. Allogeneic recipients were given methothrexate (MTX), 10mg／m^2 on day 1,3,5,7 and 11, cyclosporin A (CSP) mg／kg for GVHD prophylaxis at least 6 months. CSP dose was tapered after 2 months. Patients were nursed with strict reverse barrier techniques with all procedures

Table 1. BMT in Leukaemia

Patient	Sex	Age	Dx	Status	BMT Type
1	Male	12	T-ALL	Remission 1	Syngeneic
2	Male	12	ANLL (M1)	Remission 1	Allogeneic
3	Male	12	ANLL (M4)	Remission 1	Allogeneic
4	Male	8	C-ALL	Remission 3	Syngeneic
5	Female	15	CML	Early BC	Allogeneic

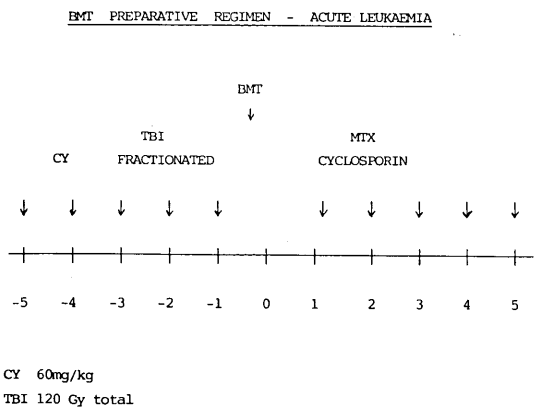

Fig. 1. BMT prepalative regimen-Acute leukamia

done aseptically. No oral gut decontamination was done. Engraftment was considered to have occurred when neutrophil count exceeds 5×10^8 /1. The outcome and complicatins of these B MTs are summarised in Table II.

Syngeneic BMT.

Two children received syngeneic BMT. Both had ALL, one T-ALL and the other C-ALL in third remission. Both are alive, however, the one with C-ALL relapsed after 9 months. He is now in remission after a further course of chemotherapy. A second BMT was considered from a HLA-compatible allogeneic sib but none was found. Both suffered from fever and mild to moderate mucositis but these symptoms subsided in the second week when engraftment took place. The boy with T-ALL developed Herpes Zooster (HZ) on day 11 which resolved with intravenous acyclovir. There were no other complications.

Allogeneic BMT

Three children received allogeneic marrow from their sibs. All three patients have died. The first allogeneic BMT (child 2) developed interstitial pneumonitis (IP) on day 105. His lung function deteriorated rapidly despite resusitative measures. A limited post-mortem confirmed presence of a IP. There was no pathological evidence of CMV but culture grew CMV. Child number 4 relapsed after a year in the CN S with subsequent relapse in the marrow. He was reinduced with high dose Ara-C and daunorubicin. He went into a partial remission (10% blasts). This was followed by high dose busulphan/CY and BMT from the original donor. Marrow engrafted but he relapsed after a month. Subsequent reinduction with chemotherapy was unsuccessful. The third allogeneic BMT was performed on a girl with CML in blast crisis. She developed BC one year post-diagnosis of CML. Remission was induced with vincristine/prednisolone and daunorubicin. She died of complications of BMT on day 9 : acute GVHD and CY/daunorubicin cardiomyopathy.

Graft-versus-host disease

GVHD did not develop in the syngeneic B MT as expected. The two patients with ANLL developed mild Grade I skin GVHD which resolved with oral prednisolone. The girl developed Grade III GVHD with the main manifestation in the skin. Mild diarrhea and mild elevation of liver enzymes were noted. She was treated with intravenous methylprednisolone 10mg/kg infused over 1 hour. She died before complete resolution of the GVHD. A limited post-mortem confirmed GVHD and marrow engraftment.

IN SUMMARY

In our limited experience, we note that BMT in children is associated with minimal compli-

Table 2. BMT Complications and outcome

Patient	Acute GVHD	Chronic GVHD	Infections	Status
1	nil	nil	Hz-Dll	Remission years
2	Grade 1-skin	Grade 1-Skin	IP-D105	Death-D105
3	nil	Facial-grade 1	nil	Relapsed 1 year
4	nil	nil	nil	Remission 9 mths
5	Grade 3-skin	-	nil	Death-D15

cations. Only one developed moderate GVHD. Except for an incidence of HZ, there was no severe bacterial or fungal infections. The children tolerated the preparative regime well. Engraftment occurred in all patients. Two deaths were related to complications of BMT : IP and acute GVHD and chemotherapy cardiomyopathy. One death was due to leukaemia relapse.

REFERENCES

1) Haghbin M, Murphy ML, Tan CC, et al. A longterm clinical follow-up of children with acute lymphoblastic leukaemia treated with intensive chemotherapy regimens. Cancer 46 : 241-252, 1980.
2) Gunz FW, Vincent PC. Towards a cure of acute granulocytic leukaemia? Leuk Res 1 : 51-66, 1977.
3) Champlin RE and Gale RP. The role of bone marrow transplantation in the treatment of hematologic malignancies and solid tumors : critical review of syngeneic, autologous and allogeneic transplants. Cancer Treat Rep 68 : 145- , 1984.
4) Morgenstern GR. Allogeneic bone marrow transplantation for acute leukaemia. Experience in 55 patients. Blut 41 : 213- 1980.
5) Thomas ED, Buckner CD, Clift RA et al. Marrow transplantation for acute nonlymph oblastic leukaemia in first remission. N Eng J Med 301 : 597-599, 1979.