Preventative policies in transfusion associated graft versus host disease in the treatment of cancer

D K H Webb

Abstract
Experience of transfusion associated graft versus host disease (TA-GvHD) and current preventative policy in 22 UK children's cancer centres was established by questionnaire. Cellular blood products were irradiated in all centres during bone marrow transplantation, but there was no consensus for children receiving standard chemotherapy. Irradiation dose varied from 1500-5000 cGy and was below 2500 cGy in 12 units. Five cases of TA-GvHD were identified; all five children died.
(*Arch Dis Child* 1994; 71: 532-533)

Transfusion associated graft versus host disease (TA-GvHD) is a rare but serious complication of blood product transfusion, with a high mortality.¹⁻³ Clinical features include skin rash, liver dysfunction, pancytopenia, fever and diarrhoea, and the disorder has followed transfusion in both immune suppressed and immune competent individuals. In cancer patients, cases have been identified in both haematological malignancy and solid tumours, but relative risk is unknown, and the best preventative practice remains undetermined. A survey of clinical practice in the treatment of childhood cancer was undertaken to determine the number of cases of TA-GvHD identified and current preventative policy.

Methods

Since 1980 over 70% of children diagnosed with cancer in Great Britain have been referred to one of 22 UK Children's Cancer Study Group centres (personal communication). Postal inquiry by structured questionnaire was used to identify details of preventative policy within these units, and cases of TA-GvHD. Data recorded included doses of irradiation administered, which blood products were considered to carry risk, which patient groups were selected for irradiated blood products, and the site of the irradiation facility. Inquiry was limited to childhood cancer, and did not include other indications for blood product irradiation, such as immune deficiency. For each case of TA-GvHD, results of confirmatory tissue biopsy, details of original diagnosis, treatment schedule and blood product irradiation practice, including dosage, were obtained.

Results

Completed questionnaires were received from all 22 centres. The date of introduction of

irradiation varied between units but irradiated products were currently provided for all children undergoing both allogeneic and autologous bone marrow transplantation, irrespective of preparatory regimen. There was variation in practice for other treatment schedules: 17 centres did not irradiate blood products during standard treatment for either haematological malignancy or solid tumours, three irradiated for children on selected protocols only (Hodgkin's disease two units, all lymphoma treatment one unit), and two irradiated for all children on cancer treatment.

Red cell, platelet, and granulocyte packs were identified to carry risk of TA-GvHD by all units while three centres also irradiated fresh, frozen plasma. Two units specified irradiation of directed donations from first degree relatives, or HLA matched platelet units. Other blood products were not considered to carry risk. Irradiation doses varied widely (table), and irradiation was undertaken on site in 12 institutions, while remaining centres obtained irradiated products from a regional transfusion centre.

Five children had TA-GvHD, proved by tissue biopsy in each case; three after chemotherapy (two Ewing's sarcoma, one Hodgkin's disease), one during allogeneic bone marrow transplantation for leukaemia, and one after autograft for rhabdomyosarcoma. The child treated by allograft had only received blood products irradiated to 1500 cGy but the other children had received unirradiated products. Both children with Ewing's sarcoma were heavily pretreated with alkylating agents, but the child with Hodgkin's disease received standard chlorambucil, vinblastine, procarbazine, and prednisolone only. All five children died due to complications of TA-GvHD.

Discussion

Graft versus host disease results from the transfusion of viable T cells, but despite estimates, the required dose of lymphocytes remains unknown and may vary according to circumstances. Besides immune suppression, other factors including shared HLA haplotype between donor and recipient appear important. In this survey TA-GvHD was well recognised as a potential hazard of transfusion by all centres and there was general agreement on those blood products which carried risk. Red cell, platelet, and granulocyte packs were uniformly identified for irradiation in at risk children, but although fresh frozen plasma was

Department of Paediatric Haematology and Oncology, Llandough Hospital, Penarth, South Glamorgan CF64 2XX

Correspondence to: Dr Webb.
Accepted 9 August 1994

Radiation doses for prevention of TA-GvHD

Dose (cGy)	No of centres
1500	8
2000	4
2500	7
3000	2
5000	1

irradiated in several centres, evidence implicating this product is weak.⁴ Although several centres identified directed donations for irradiation, this donation practice is uncommon in the UK, but irradiation of HLA matched platelet packs appears sensible practice, and is likely to become more widespread.

Irradiation practice was subject to considerable variation especially in administered dose. Current recommendations in the US are for 2500 cGy due to TA-GvHD after transfusion of products irradiated at lower doses, and one child in this survey developed TA-GvHD despite irradiation of all transfused products to 1500 cGy; at present 12 UK centres irradiate to less than 2500 cGy and standardisation of national practice is required.

All centres irradiated cellular blood products for children treated by bone marrow transplant, although there was less agreement for other treatment. Two units introduced irradiation for products transfused to children with lymphoma, and one unit for all children on chemotherapy, after cases of TA-GvHD. Nationally, however, only three cases were identified outside bone marrow transplantation, and with over 12 000 children diagnosed and treated at UK Children's Cancer Study Group centres since 1980, the incidence of

recognised cases is very low and these data do not support routine irradiation of blood products in children receiving standard chemotherapy. Neither are there adequate data from this study to identify any subgroup of children on standard chemotherapy who are at increased risk. However, it remains possible that mild cases pass unrecognised, due to the similarity between clinical features of TA-GvHD and other complications of cancer treatment and the consequences of increased treatment intensity regarding incidence of TA-GvHD are unclear. A high level of suspicion, investigation by tissue biopsy, and a national registry of proved cases would all aid study of these aspects.

I am grateful to consultant staff in the 22 UK Children's Cancer Study Group centres for completion of questionnaires.

- 1 Anderson KC, Goodnough LT, Sayers M, *et al.* Variation in blood component irradiation practice; implications for prevention of transfusion associated graft versus host disease. *Blood* 1991; 77: 2096–102.
- 2 Greenbaum BH. Transfusion associated graft versus host disease; historical perspectives, incidence, and current use of irradiated blood products. *J Clin Oncol* 1991; 9: 1889–902.
- 3 Flidner V, Higby DJ, Kim U. Graft versus host reaction following blood product transfusion. *Am J Med* 1982; 72: 951–61.
- 4 Linden JV, Pisciotto PT. Transfusion associated graft-versus-host disease and blood irradiation. *Transfus Med Rev* 1992; vi: 116–23.